

# **Research Integrity and Ethical Biomedical research on humans**

by

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## DEDICATION

First and foremost, I would like to give thanks to the All Mighty. This dissertation is dedicated to my amazing wife Azraa Janse van Vuuren. Without her love, support, encouragement and patience, the writing up of this dissertation would not have been possible.

## SUMMARY

Research misconduct is a global problem that tarnishes the reputation of researchers and research institutions and inevitably compromises the independence, integrity and credibility of the scientific record. Biomedical researchers like all other professionals are susceptible to pressures and temptations, which may result in them engaging in questionable research practices or deliberate misconduct. In order to promote ethical research behaviour and foster scientific integrity, scientists need to be equipped to deal with the ethical dilemmas they may face when conducting research on/relating to human participants. Preventing research misconduct is the first step in preserving and restoring the integrity of the scientific record. Understanding the causes of and contributing factors associated with research misconduct are essential in devising preventative strategies. Furthermore, the scientific literature is only as reliable as the trustworthiness and calibre of the research team, therefore the development and training of ethical, adequately qualified, self-reflective researchers is crucial in fighting the battle against scientific misconduct. With reports of misconduct on the increase in South Africa and elsewhere, there is clearly a need to better equip researchers with the knowledge they need to conduct responsible, ethical research on humans and to bring to their attention the most common forms of research misconduct (be it intentional or not) that is plaguing the scientific community.

## ACRONYMS

CADC: Complaints and Advisory Disciplinary Committee

CONSORT: Consolidated Standards of Reporting Trials

COPE: The Committee of Publication Ethics

DHET: Department of Higher Education and Training

EPPS: The National Department of Health's Ethics in Health Research, 2nd edition

FFP: Fabrication, Falsification, and Plagiarism

HHS: United States Department of Health and Human Services

ICMJE: International Committee of Medical Journal Editors

MHCA: Mental Health Care Act 17 of 2002

MRC: Medical Research Council

NHA: National Health Act 61 of 2003

NHREC: National Health Research Ethics Council

NRF: National Research Foundation

ORI: The Office of Research Integrity

POPI: Protection of Personal Information Act 4 of 2013

QRP: Questionable research practices

RCR: Responsible conduct of research

REC: Research Ethics Committee

SOP: Standard Operating Procedures

ToR: Terms of reference

WAME: World Association of Medical Editors

WHO: World Health Organisation

# CHAPTER 1

## INTRODUCTION

### 1.1 BACKGROUND

Research is defined as the systematic, rigorous investigation of a situation or problem in order to generate new knowledge, validate existing knowledge or reach new conclusions.<sup>1</sup> Biomedical research refers to the study of the processes of life, the prevention and treatment of disease, and the genetic and environmental factors associated with disease and health, through careful experimentation, observation, laboratory work, analysis, and testing.<sup>2</sup>

The terms 'Biomedical research', 'Medical research' and 'Health research' are synonymous and are often used interchangeably. Biomedical research may be broadly divided into three categories: basic research; applied research (including epidemiological research) and clinical research.<sup>3</sup> Basic research is fundamental in nature with its goal being the improvement of basic scientific knowledge by expanding our understanding about how processes in living organisms develop and function.<sup>4</sup> Applied research entails the application of existing knowledge, in order to address a specific biomedical problem.<sup>5</sup> It can involve research on humans, animals, tissue cultures and computer models.<sup>6</sup>

Clinical research builds upon the knowledge acquired from applied and basic research, and is mainly conducted on human subjects, with the objective of directly improving healthcare.<sup>7</sup> Clinical trials are a well-known type of clinical research. In clinical trials patients volunteer to

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<sup>1</sup> The Free Dictionary by Farlex website (2015) Available online: <http://medical-dictionary.thefreedictionary.com/research> [Accessed 09/02/2016]; Oxford University Press website "Oxford Dictionaries" (2015) Available online: <http://www.oxforddictionaries.com/definition/english/research> [Accessed 09/02/2016].

<sup>2</sup> California Biomedical Research Association website "What is Biomedical Research?" (2015) Available online: <http://ca-biomed.org/pdf/media-kit/fact-sheets/FS-WhatBiomedical.pdf> [Accessed 09/02/2016]; States United for Biomedical Research website "Biomedical Research Definitions" (2016) Available online: <http://www.statesforbiomed.org/content/biomedical-research-definitions> [Accessed 08/03/2016]; New Jersey Association for Biomedical Research website "Biomedical Research Definitions" (2016) Available online: <http://njabr.com/education/general-background-on-biomedical-research/biomedical-research-definitions/> [Accessed 08/03/2016].

<sup>3</sup> New Jersey Association for Biomedical Research website "Biomedical Research Definitions" (2016).

<sup>4</sup> California Biomedical Research Association website "What is Biomedical Research?" (2015); New Jersey Association for Biomedical Research website "Biomedical Research Definitions" (2016).

<sup>5</sup> California Biomedical Research Association website "What is Biomedical Research?" (2015); New Jersey Association for Biomedical Research website "Biomedical Research Definitions" (2016).

<sup>6</sup> New Jersey Association for Biomedical Research website "Biomedical Research Definitions" (2016).

<sup>7</sup> *Ibid.*

participate in studies to test the efficacy and safety of new medical interventions.<sup>8</sup>

S 72(7) of the National Health Act 61 of 2003 (NHA) defines a clinical trial as “a systematic study involving human subjects that aims to answer specific questions about the safety or efficacy of a medicine or method of treatment”.<sup>9</sup> Clinical trials are therefore not limited to the study of drugs, and can also include other treatment interventions.<sup>10</sup> In South Africa, a summary of the results of every clinical trial conducted in the country must be submitted to the South African Clinical Trial Register within a year of completion.<sup>11</sup>

Research in South Africa has witnessed substantial growth since the dawn of the new millennium. This drive has been influenced strongly by the establishment of the National Research Foundation (NRF) in 1999. The Department of Higher Education and Training (DHET) also awards subsidies for publications appearing in accredited South African journals, as well as international, ISI and IBSS accredited journals, books and book chapters, so further incentivising research outputs. It must however, be mentioned that in South Africa, the culture of publishing is not prevalent across all universities and research institutions.<sup>12</sup> Young academics/researchers are placed under immense pressure, and are forced to ‘publish or perish’.<sup>13</sup> With a massive drive to increase research output, young researchers lacking the skills-set and knowledge particularly when conducting biomedical research may end up facing moral and ethical challenges.

For the purposes of this dissertation, the focus will be on research conducted on or relating to human participants. There are various laws, regulations and guidelines (both locally and internationally) that govern research on humans. In South Africa, we have a supreme Constitution, the NHA and its regulations, the Children’s Act, case law as well as national ethical research guidelines such as: the Department of Health’s “Guidelines for good practice in the conduct of clinical trials on human participants in South Africa”; the Department of Health’s “Ethics

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<sup>8</sup> Sharyl J. Nass (2009) "Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research" 19; S 72(7) of the National Health Act of 2003.

<sup>9</sup> National Health Act 61 of 2003.

<sup>10</sup> Dhai & Cleaton-Jones (2011) “The Ethics of Research” In Dhai & McQuoid-Mason eds. "Bioethics, Human Rights & Health Law: Principles & Practice" 170.

<sup>11</sup> Department of Health “South African Good Clinical Practice Guidelines Second Edition” (2006) South Africa 55.

<sup>12</sup> Inglesi-Lotz & Pouris "Scientometric impact assessment of a research policy instrument: the case of rating researchers on scientific outputs in South Africa" (2011) 88, 3 *Scientometrics* 747-760.

<sup>13</sup> Neill "Publish or perish, but at what cost?" (2008) 118, 7 *The Journal of Clinical Investigation* 2368; Altman "The scandal of poor medical research" (1994) 308 *British Medical Journal* 283-284; Khanyile *et al* "Research integrity and misconduct: a clarification of the concepts" (2006) 29, 1 *Curationis* 40-45.



in Health Research: Principles, Structures and Processes guideline”; the HPCSA’s “General Ethical Guidelines for Health Researchers”; and the MRC’s “Guidelines on Ethics for Medical Research”.<sup>14</sup>

The most important international guidelines that are of relevance include: the “Nuremberg Code”; the “Belmont Report”; the World Medical Association’s “Declaration of Helsinki”; the Council for International Organizations of Medical Science’s “International Ethical Guidelines for Biomedical Research involving Human Subjects”, and the Nuffield Council on Bioethic’s “The ethics of research related to healthcare in developing countries” of 2002 (as well as its follow up report in 2005).

The Office of Research Integrity (ORI) which organisationally falls under the United States Department of Health and Human Services (HHS) is one example of a well-established statutory body in the USA whose influence and control have extended globally.

In South Africa, under the NHA, the National Health Research Ethics Council (NHREC) was established. Some of its functions include, but are not limited to: determining guidelines for the functioning of Research Ethics Committees (RECs); registering and auditing RECs; adjudicating complaints against RECs; setting norms and standards for conducting research on humans and animals; advising the national and provincial departments on any ethical issues concerning health research; and instituting disciplinary actions against any person found to be in violation of any legal, ethical or professional rule, standards or guidelines, set for the conducting of research in terms of the regulations set out in the NHA.<sup>15</sup>

Furthermore, Section 73(1) of the NHA states that: “Every institution, health agency and health establishment at which health research is conducted, must establish or have access to a health research ethics committee, which is registered with the National Health Research Ethics Council.”<sup>16</sup> Under the NHREC a Complaints and Advisory Disciplinary Committee (CADC) was also established, and in 2012 developed and published guidelines for the management of complaints related to health research misconduct and ethics.

Various academic institutes in South Africa have implemented sound and well-drafted policies on research ethics. These institutions together

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<sup>14</sup> Nienaber "Law and Ethics in the context of Research on Humans in South Africa" (2015) *PBL 811 Lecture : University of Pretoria*.

<sup>15</sup> S 72(6) of the National Health Act 61 of 2003.

<sup>16</sup> S 73(1) of the National Health Act 61 of 2003.

with research ethics committees (RECs) and the NHREC, have a pivotal role in promoting research integrity and responsible research conduct.<sup>17</sup>

In order to promote ethical research behaviour and foster scientific integrity, researchers should have a good understanding of the concepts of 'unethical research practices' and 'research misconduct'. Over the last two decades, the research community has reached consensus in broadly categorising research behaviour into three groups: deliberate misconduct often defined as fabrication, falsification, and plagiarism (FFP); questionable research practices (QRP); and responsible conduct of research (RCR).<sup>18</sup> RCR is the ideal standard that researchers should adhere to, FFP are unethical research practices that the researcher should avoid, and QRP are behaviours that are neither RCR or FFP, the so called 'grey areas' that require clarity.<sup>19</sup>

Research misconduct is a global problem, and with an international and national drive to increase research outputs, reports of misconduct are on the increase in South Africa and elsewhere.<sup>20</sup> Biomedical researchers need to be equipped to deal with the ethical dilemmas they may encounter when conducting research on/relating to human participants. Furthermore, they have to be familiar with current legislation, regulations and guidelines governing this type of research in order to minimise research misconduct and improve the quality and sustainability of research.<sup>21</sup>

## 1.2 RATIONALE AND PURPOSE OF THE STUDY

The aims and objectives of the study are:

1.2.1 To understand the nature of and complexities associated with research involving human participants.

1.2.2 To clarify and interpret current legislation, policies and guidelines regulating research on/relating to human participants.

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<sup>17</sup> Horn (2013) 6, 1 *South African Journal of Bioethics and Law* 21-24.

<sup>18</sup> Mitcham (2003) 9, 2 *Science and Engineering Ethics* 273-290; Steneck "Fostering integrity in research: Definitions, current knowledge, and future directions" (2006) 12, 1 *Science and Engineering Ethics* 53-74; Galland "Developing, Sharing and Promoting Best Practices" (2010) *2nd World Conference on Research Integrity, Singapore*; Steneck "The Responsible Conduct of Basic and Clinical Research" (2005) *International Bioethics Conference, Poland*.

<sup>19</sup> Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>20</sup> Mitcham (2003) 9, 2 *Science and Engineering Ethics* 273-290; Horn (2013) 6, 1 *South African Journal of Bioethics and Law* 21-24; Ana et al (2013) 10, 3 *PLoS Med* 1-5.

<sup>21</sup> Neill (2008) 118, 7 *The Journal of Clinical Investigation* 2368.

1.2.3 To promote and reinforce research integrity and responsible publication ethics.

1.2.4 To clarify and interpret current best practices, policies and guidelines relating to the management of research misconduct in a South African setting.

### **1.3 RESEARCH QUESTIONS**

1.3.1 What constitutes ethical research on humans?

1.3.2 What are the applicable regulations, laws and guidelines governing biomedical/health research on humans both locally and internationally?

1.3.3 What are the current best practices on publication ethics?

1.3.4 What is research/scientific misconduct and how should it be managed?

### **1.4 RESEARCH METHODOLOGY AND LIMITATIONS**

A desktop review of the relevant statutes, local and international guidelines and policies, relevant textbooks and journal articles was conducted. Since this is a desktop review, no ethical clearance was required.

The following sources were canvassed:

- Various local and international guidelines and policies relating to biomedical research;
- South African Legislation and the Constitution of the Republic of South Africa, 1996;
- Textbooks;
- Journal articles;
- Conference presentations/proceedings; and
- Google scholar searches using the words: 'ethical research on humans', 'research misconduct' and 'publication ethics'

No data was collected or analysed in order to gauge the level of knowledge among South African biomedical researchers on this particular topic. However, based on the available literature and the increase in reports of misconduct in South Africa, this increase might

be associated with inexperience and a lack of knowledge when conducting research on humans.<sup>22</sup>

## 1.5 DEFINITIONS OF KEY TERMS, CONCEPTS AND VARIABLES

Ethics-: “a study of morality involving a careful, systematic reflection on and analysis of actions and behaviour”<sup>23</sup> (ie it deals with the moral choices people make and the analysis of what constitutes ‘right’ or ‘wrong’ actions).<sup>24</sup>

Bioethics-: “A field of ethical enquiry that examines ethical issues and dilemmas arising from health, health care and research involving humans.”<sup>25</sup>

Biomedical Research-: “refers to the investigation of the biological process and the causes of disease through careful experimentation, observation, laboratory work, analysis, and testing.”<sup>26</sup>

Researcher-: “A person who engages in the methodical and systematic investigation of hypotheses with the goal of contributing to new knowledge.”<sup>27</sup>

Research protocol/proposal-: “A document written by the investigator(s), which should contain a project summary ; general information ; background rationale ; references and literature review ; study goals and objectives ; study design ; methodology ; safety considerations ; follow-up ; data management considerations and statistical analysis ; quality assurance ; expected outcomes of the study ; dissemination of results and publication policy ; duration of the project ; problems anticipated ; project management ; ethical considerations ; informed-consent documents ; budget ; funding organizations ; collaborations ; curriculum vitae of each investigator ; list of all current projects ; duration and percentage of time spent on this project ; any financing or insurance.”<sup>28</sup>

Research Misconduct-: The US Federal Policy on Research Misconduct simply defines research misconduct as “falsification or plagiarism in proposing, performing or reviewing research, or in the reporting of

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<sup>22</sup> Mitcham (2003) 9, 2 *Science and Engineering Ethics* 273-290; Horn (2013) 6, 1 *South African Journal of Bioethics and Law* 21-24; Ana *et al* (2013) 10, 3 *PLoS Med* 1-5.

<sup>23</sup> Dhali & McQuoid-Mason (2011) "Bioethics, Human Rights & Health Law: Principles & Practice" 3.

<sup>24</sup> *Ibid.*

<sup>25</sup> Coleman *et al* (2009) "Research ethics committees: Basic concepts for capacity-building" 5.

<sup>26</sup> California Biomedical Research Association website "What is Biomedical Research?" (2015).

<sup>27</sup> Coleman *et al* (2009) 6.

<sup>28</sup> *Ibid.*

research results”<sup>29</sup>, however other institutions have correctly included behaviours such as: a material failure to comply with governmental regulations; unauthorised use of confidential information, and retaliation or threat of retaliation against persons involved in the allegation or investigation of misconduct, in the definition.<sup>30</sup>

Scientific/Research Integrity -:“The use of honest and verifiable methods in proposing, performing and evaluating research and in reporting research results, with particular attention to adherence to rules, regulations, guidelines and commonly accepted professional codes or norms.”<sup>31</sup>

Research Ethics -: “Research behaviour viewed from the perspective of moral principles.”<sup>32</sup>

Research ethics committee-: A specialised group of individuals that review proposed studies involving human participation in order to ensure that they conform to relevant and established international and local ethical guidelines.<sup>33</sup> They also monitor on-going studies, and where relevant take part in follow-up action and surveillance after a study is completed.<sup>34</sup>

Publications-: “includes the full range of formats published in peer-reviewed journals (for example, original research articles, short reports, reviews, or letters to the editor) and “presentations” to include abstracts, posters, and slides for oral presentations at scientific congresses.”<sup>35</sup>

Expression of Concern -: is issued when an editor suspect’s scientific misconduct in a publication, but the outcome of an investigation is pending, or an investigation has not begun.<sup>36</sup>

Retraction -: is issued when an investigation has concluded that a publication contains fabricated or falsified data, or has been plagiarised, then a journal must issue a (ie this tells the scientific community to ignore the publication).<sup>37</sup>

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<sup>29</sup> American Physical Society "U.S. Federal Policy on Research Misconduct" (2002) Available online: <http://www.aps.org/policy/statements/federalpolicy.cfm> [Accessed 15/07/15].

<sup>30</sup> As referenced in Giannobile *et al* (2010) "Clinical Research in Oral Health " 70.

<sup>31</sup> Steneck (2005) *International Bioethics Conference, Poland*.

<sup>32</sup> Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>33</sup> Coleman *et al* (2009) 6.

<sup>34</sup> *Ibid*.

<sup>35</sup> Battisti *et al* "Good publication practice for communicating company-sponsored medical research: GPP3" (2015) 163, 6 *Annals of Internal Medicine* pp.461-464.

<sup>36</sup> Sox & Rennie "Research misconduct, retraction, and cleansing the medical literature: lessons from the Poehlman case" (2006) 144, 8 *Annals of Internal Medicine* 609-613.

<sup>37</sup> *Ibid*.

Correction-: is issued by the editor of a journal to correct a mistake, either by substituting correct information, or by asking the scientific community to disregard specified parts of a publication.<sup>38</sup>

Retraction Index -: An index sometimes used by scientific journals that represents the number of retractions over a 10 year period, multiplied by 1,000 divided by the number of published articles with abstracts in the same 10 year period.<sup>39</sup>

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<sup>38</sup> *Ibid.*

<sup>39</sup> Katavić "Retractions of scientific publications: responsibility and accountability." (2014) 24, 2 *Biochemia medica* 217-222.

## CHAPTER 2: RESPONSIBLE AND ETHICAL BIOMEDICAL RESEARCH ON HUMANS

### 2.1 KEY ETHICAL PRINCIPLES IN RESEARCH

The three basic ethical principles summarised in the Belmont Report of 1979, ie, 'respect of persons', 'beneficence' and 'justice' form the basic moral framework around which regulations and guidelines governing biomedical research involving human subjects around the world, are drafted.<sup>40</sup>

Any biomedical research that is conducted on humans must involve the integration of key ethical and legal principles in order to protect the rights of participants, while still significantly contributing to the benefit of science and society as a whole.<sup>41</sup> Some basic ethical guidelines include: protecting both participants and researchers from harm; obtaining informed consent and respecting confidentiality; balancing benefits and risk; respecting the privacy of participants, as well as exercising honesty and integrity when conducting and publishing research.<sup>42</sup> These guidelines are centred on the 'Principle-based' or 'Principlism' approach in bioethics, introduced by Tom Beauchamp and James Childress in 1979.<sup>43</sup> The key ethical principles of Principlism include: respect for autonomy, non-maleficence, beneficence and justice.<sup>44</sup> These four principles also form the basis for ethical review of research protocols by most RECs.

Respect for individual autonomy mainly deals with consent and comprehension among other ideals. In relation to research ethics, it essentially means that an individual should first be given sufficient information about a study or trial (and time to understand this information), before any voluntary decision regarding his/her participation is made.<sup>45</sup> Moreover, participants who lack the capacity to

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<sup>40</sup> The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research "The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research" (1979) Available online: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html> [Accessed 15/03/16].

<sup>41</sup> Moodley (2011) "Medical Ethics, Law and Human Rights: A South African Perspective" 317.

<sup>42</sup> Slowther *et al* "Research governance: ethical issues" (2006) 99, 2 *Journal of the Royal Society of Medicine* 65-72.

<sup>43</sup> Moodley (2011) 37; WHO "Casebook on Ethical Issues in International Health Research" 198.

<sup>44</sup> Moodley (2011) 37; Avasthi *et al* "Ethics in medical research: General principles with special reference to psychiatry research" (2013) 55, 1 *Indian Journal of Psychiatry* 86-91; Council for International Organizations of Medical Sciences "International Ethical Guidelines for Biomedical Research Involving Human Subjects" (2002) 17-18; WHO "Casebook on Ethical Issues in International Health Research" (2009) 198.

<sup>45</sup> Avasthi *et al* (2013) 55, 1 *Indian Journal of Psychiatry* 86-91; Dhai & Cleaton-Jones (2011) 174; WHO "Casebook on Ethical Issues in International Health Research" (2009) 208.

make informed choices should be protected against harm arising from these choices.<sup>46</sup> Other constructs falling under the ambit of ‘autonomy’ include: respect for persons; confidentiality; and avoidance of coercion.<sup>47</sup> Respect for persons emphasises that the well-being and dignity of the research participants are essential.<sup>48</sup> This principle is, however, also applicable to the researchers themselves, and includes professional interests such as authorship and intellectual property rights.<sup>49</sup>

Non-maleficence means ‘first do no harm’, when applying this principle to research ethics, one can say that researchers should be competent and adequately trained and the research design should be sound in order to protect research participants from any harm (ie the obligation to avoid causing harm to others).<sup>50</sup> When conducting any form of biomedical research, the safety and well-being of research participants is paramount. The protection of researchers themselves and minimizing their exposure to harm is also encompassed in this principle.<sup>51</sup> Furthermore, the risks of research should be reasonable in the light of the expected benefits.<sup>52</sup>

The principal of ‘Beneficence’ refers to the obligation to ‘do good’ for others.<sup>53</sup> The ultimate goal of research involving human beings should be promoting the well-being of the research participants as well as society as a whole.

Last but not least, “Justice refers to the ethical obligation to treat each person in accordance with what is morally right and proper and to give each person what is due to him or her”.<sup>54</sup> When applied to research ethics, this principle implies that after the research intervention, “participants and/or communities should be better off or no worse off”<sup>55</sup> than before. Participants should also be fairly compensated for any expenses they might incur as a result of participating in research, and populations that are excluded from research should not be

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<sup>46</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” (2015) South Africa 15.

<sup>47</sup> Avasthi *et al* (2013) 55, 1 *Indian Journal of Psychiatry* 86-91; Slowther *et al* (2006) 99, 2 *Journal of the Royal Society of Medicine* 65-72.

<sup>48</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 15.

<sup>49</sup> *Ibid.*

<sup>50</sup> Dhai & Cleaton-Jones (2011) 175; Avasthi *et al* (2013) 55, 1 *Indian Journal of Psychiatry* 86-91; WHO “Casebook on Ethical Issues in International Health Research” (2009) 208; Coleman *et al* (2009) 19.

<sup>51</sup> Slowther *et al* (2006) 99, 2 *Journal of the Royal Society of Medicine* 65-72.

<sup>52</sup> WHO “Casebook on Ethical Issues in International Health Research” (2009) 208.

<sup>53</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 14; WHO “Casebook on Ethical Issues in International Health Research” (2009) 208; Coleman *et al* (2009) 19.

<sup>54</sup> WHO “Casebook on Ethical Issues in International Health Research” (2009) 208.

<sup>55</sup> Dhai & Cleaton-Jones (2011) 175; Avasthi *et al* (2013) 55, 1 *Indian Journal of Psychiatry* 86-91.



disadvantaged, as a result thereof.<sup>56</sup> Distributive justice deals with equality and a fair distribution of benefits and burdens among participants, communities and society in general ie there should be reasonable likelihood that research participants as well as communities from which they were selected will derive either long or short-term benefits as a result of the research.<sup>57</sup>

Whenever an ethical dilemma needs to be resolved, be it during ethical review by a REC or in the field while conducting research, the application of these four ethical principles of moral deduction is indispensable.

## **2.2 THE APPLICABLE STATUTES, REGULATIONS AND GUIDELINES GOVERNING BIOMEDICAL RESEARCH ON HUMANS**

Unfortunately history has been plagued with human rights atrocities committed in the name of 'medical research'. From the flagitious Nazi medical experiments of the third Reich, to the notorious Tuskegee and Guatemalan syphilis studies conducted by American scientists.<sup>58</sup> From 1932 to 1972, six hundred impoverished African-American males from Tuskegee, Alabama were enrolled in a study titled: "Tuskegee study of Untreated Syphilis in the Negro Male" without their consent.<sup>59</sup> What made matters worse, was that even after the discovery of penicillin in 1945, treatment was deliberately withheld in order to study the natural progression of the disease.<sup>60</sup> As a result of the Tuskegee syphilis study, an authoritative document relating to ethical research on humans, The Belmont Report was published in 1979.<sup>61</sup> The Belmont Report is based on three basic ethical principles ie respect for persons; beneficence; and justice, and how these principles can be applied when conducting research on humans.

After World War II, the Nuremberg trials exposed the research atrocities of the Nazi regime, and in 1947 the Nuremberg Code was developed.<sup>62</sup> The Nuremberg Code is based on ten ethical principles and is considered to be the "founding document of contemporary

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<sup>56</sup> Dhai & Cleaton-Jones (2011) 175; Slowther *et al* (2006) 99, 2 *Journal of the Royal Society of Medicine* 65-72.

<sup>57</sup> Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 14-15; WHO "Casebook on Ethical Issues in International Health Research" (2009) 208; Coleman *et al* (2009)

<sup>58</sup> Moodley (2011) 318-319.

<sup>59</sup> Guraya *et al* "Ethics in medical research" (2014) 2, 3 *Journal of Microscopy and Ultrastructure* 121-126; Moodley (2011) 318-319.

<sup>60</sup> Moodley (2011) 318-319

<sup>61</sup> *Ibid.* 318-319.

<sup>62</sup> Dhai & Cleaton-Jones (2011) 167; Guraya *et al* (2014) 2, 3 *Journal of Microscopy and Ultrastructure* 121-126; Moodley (2011) 319-320.

research ethics”<sup>63</sup>. Another critical set of guidelines drawn up by the World Medical Association is the Declaration of Helsinki of 1964. It has been described as an “expansion of the Nuremberg Code”<sup>64</sup> and has been amended a number of times, the most recent version was published in 2013. The South African Medical Association and all RECs in the country endorse the latest version of the Declaration of Helsinki, and any biomedical research that is conducted in the country must adhere to its guiding principles.<sup>65</sup> It was these three founding documents mentioned above that paved the road for ethical biomedical research in the world. There are numerous other ethical guidelines/policies governing research on humans that have been published around the world, a select few are listed in table 1 (Annexure A).

When canvassing the relevant statutes, regulations and guidelines governing biomedical research on humans in South Africa (table 2) a layered approach must be followed. The starting point will always be the Constitution on the Republic of South Africa, 1996. Chapter 2, Bill of Rights, Section 12 (b)(c) states that:

“Everyone has the right to freedom and security of the person, which includes the right to security in and control over their body; and not to be subjected to medical or scientific experiments without their informed consent.”<sup>66</sup>

However, Section 16 (d) also allows for academic freedom and freedom of scientific research.<sup>67</sup>

The most important piece of legislation governing research on humans in South Africa is the NHA. According to The NHA, health research includes any research which contributes to knowledge of -

- “(a) the biological, clinical, psychological or social processes in human beings;
- (b) improved methods for the provision of health services;
- (c) human pathology;
- (d) the causes of disease;
- (e) the effects of the environment on the human body;
- (f) the development or new application of pharmaceuticals, medicines and related substances; and
- (g) the development of new applications of health technology”<sup>68</sup>

<sup>63</sup> Guraya *et al* (2014) 2, 3 *Journal of Microscopy and Ultrastructure* 121-126.

<sup>64</sup> Dhai & Cleaton-Jones (2011) 167.

<sup>65</sup> Moodley (2011) 321.

<sup>66</sup> S 12 (b)(c) of the Constitution on the Republic of South Africa, 1996.

<sup>67</sup> S 16 (d) of the Constitution on the Republic of South Africa, 1996.

Chapter 2 Section 11 “Health Services for experimental or research purposes”, subsections (1) and (2) of the NHA also states that:

“1) Before a health establishment provides a health service for experimental or research purposes to any user and subject to subsection (2), the health establishment must inform the user in the prescribed manner that the health service is for experimental or research purposes or part of an experimental or research project.

(2) A health establishment may not provide any health service to a user for a purpose contemplated in subsection (1) unless the user, the health care provider primarily responsible for the user's treatment, the head of the health establishment in question and the relevant health research ethics committee, or any other person to whom that authority has been delegated, has given prior written authorisation for the provision of the health service in question.”<sup>69</sup>

Chapter 8 “Control of use of Blood, Blood Products, Tissue and Gametes in Humans” and Chapter 9 “National Health Research and Information” of the NHA also relate directly to biomedical research in South Africa.

Most recently, Government Notice R719 “Regulations Relating to Research with Human Participants” was published in Government Gazette 38000 dated 19 September 2014. This regulation includes important definitions such as ‘therapeutic research’ and ‘non-therapeutic research’ and other critical subjects/themes such as: principles guiding research with human participants; obligations of researchers; vulnerable study participants; and informed consent in research.<sup>70</sup> According to Section 2 of these regulations, health research involving human participants must:

- “(a) comply with the Department of Health national ethical guidelines for research with human participants at a minimum;
- (b) be responsive to health needs or priorities of the population, participating community or proposed participants;
- (c) have a valid scientific methodology and be likely to provide answers for the specific research questions that are posed;
- (d) include a favourable risk-benefit analysis;
- (e) ensure that the recruitment and selection process is just and fair;
- (f) be undertaken with appropriate consent processes;
- (g) undergo independent review by a registered health research ethics committee;

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<sup>68</sup> S 1 of the National Health Act 61 of 2003.

<sup>69</sup> S 11 (1)(2) of the National Health Act 61 of 2003.

<sup>70</sup> Government Notice R719 “Regulations relating to Research with Human Participants” published in published in Government Gazette 38000 dated 19 September 2014.

- (h) respect participants' rights, including but not limited to rights to dignity, privacy, bodily integrity and equality;
- (i) make provision for compensation for research-related injury, for more than minimal risk research; and
- (j) be managed by a lead researcher, or person with similar standing or title, with suitable experience and qualifications.”<sup>71</sup>

Important national guidelines and policies include: The National Department of Health’s “Ethics in Health Research Principles, Processes and Structures”, 2nd edition (EPPS) published in 2015; and the first edition of the “Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa”, published in 2000 followed the second edition which was published in 2006.

The South African Medical Research Council's (MRC) has also published guidelines on ethical medical research (table 2). These guidelines are however, outdated and should only be utilised for background information. The South African MRC recommends the use of the EPPS instead.<sup>72</sup> The Health Professions Council of South Africa (HPCSA) also has a number of guidelines on ethical rules, regulations and policies, those relevant to biomedical research are listed in table 2.

There are several generic subjects/themes relating to research on humans that appear in all of the above mentioned documents. These topics will be discussed further in the following section. Research misconduct and publication ethics will be canvassed in chapter 3.

## 2.3 RESEARCH ON HUMANS

### 2.3.1 CONSENT AND COMPREHENSION

According to EPPS, consent is defined as an “indication of an agreement to participate in research, based on adequate knowledge and understanding of relevant information, and freely given”.<sup>73</sup> The terms ‘Informed Consent’ and ‘Consent’ are often used interchangeably. In the present day and age both nationally and internationally, research cannot be legally conducted on humans without obtaining voluntary informed consent. Where individuals are not capable of giving informed consent, permission of a legally authorised representative should be sought, as per statutory obligation.<sup>74</sup> Generally speaking and as per definition, for consent to be valid the

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<sup>71</sup> *Ibid.*

<sup>72</sup> As stated on the MRC website: <http://www.mrc.ac.za/ethics/ethics.htm> [Accessed 14/10/2016]

<sup>73</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 77.

<sup>74</sup> Council for International Organizations of Medical Sciences (2002). 32.

following medico-legal criteria have to be met: comprehension or understanding; capacity; full disclosure and voluntariness.<sup>75</sup> First and foremost consent must be voluntary and uncoerced. Furthermore participants should be made aware that they have a right not to participate in research, and that they have a right to withdraw at any given time without the risk of penalty.<sup>76</sup> It is logical to assume that consent cannot be voluntary or uncoerced if it is uninformed.

Therefore, participants must be informed *inter alia*, about: the nature, purpose and expected benefits of the research; the roles and responsibilities of both the researchers and the participants; potential risks associated with participation in the research; alternatives to participation in the research; and that the research has been approved and registered by a REC.<sup>77</sup>

Moreover, the informed consent process should be dynamic and interactive (ie, information should be updated throughout the duration of the study in order to ensure participants always remain ‘informed’).<sup>78</sup> It is also critical that participants understand and comprehend the information that is being explained to them, this can be achieved by translating this information to the participants’ language of choice.<sup>79</sup> Moreover, this information should be conveyed in a manner that suits the participant’s level of understanding.

One exception where informed consent or re-consent may be waived is the use of data in the form of records or biological material for research purposes. Biological materials and records may be collected for diagnostic, therapeutic or health research purposes.<sup>80</sup> In situations where data is collected from records or stored biological material needs to be utilised, RECs may approve access to identifiable or potentially identifiable data or biological materials without the need for consent or re-consent.<sup>81</sup> It is, however, pivotal for RECs to assess whether the nature of the planned usage is/was adequately explained to the participants when their informed consent was initially obtained. If

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<sup>75</sup> As cited in Dhai & McQuoid-Mason (2011) 71.

<sup>76</sup> Government Notice R719 “Regulations Relating to Research with Human Participants” published in Government Gazette 38000 dated 19 September 2014; Department of Health “South African Good Clinical Practice Guidelines Second Edition” 70.

<sup>77</sup> Government Notice R719 “Regulations Relating to Research with Human Participants” published in Government Gazette 38000 dated 19 September 2014; Council for International Organizations of Medical Sciences (2002). 37-39.

<sup>78</sup> Coleman *et al* (2009) 43; Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 74.

<sup>79</sup> Department of Health “South African Good Clinical Practice Guidelines Second Edition” 11.

<sup>80</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 42.

<sup>81</sup> Council for International Organizations of Medical Sciences (2002). 35-36; Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 41.

deemed necessary and depending on the circumstances RECs may require re-consent.<sup>82</sup>

There are three major types of consent relating to patient records and biological materials in biomedical research:

A practical example of the use biological tissue that is anonymous and would not place any individual, family or community at risk of social, psychological, legal or economic harm would be the use of extracted wisdom teeth in dental materials research.

### 2.3.2 UNFAIR INDUCEMENT/COERCION AND EXPLOITATION

There are complex ethical considerations at play when deciding whether participants should be compensated for subjecting themselves to research or clinical trials. When incentives are offered to prospective research participants there must be careful consideration so as not to promote unfair inducement. Financial compensation should not be too large and medical treatment offered should not be too extensive, ie patients should not be persuaded to take undue risks or volunteer against their better judgement, because they are being given an offer that 'they cannot refuse'.<sup>83</sup>

In a South African setting where unemployment and poverty are prevalent, what is considered to be 'an offer one cannot refuse' is very different for an underprivileged individual from an informal settlement compared to the average working class individual residing in the urban suburbs. Any form of compensation individuals receive for participating in research, must be included in the research protocol and approved by the relevant REC.

Generally speaking, participants should be compensated for their time, inconvenience and expenses (TIE).<sup>84</sup> This approach is aimed at minimizing unfair inducement, as compensation is linked to actual expenses or inconveniences incurred.<sup>85</sup>

Minors and individuals with intellectual or mental impairments may be susceptible exploitation by their guardians for financial benefit.<sup>86</sup> In

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<sup>82</sup> Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 42.

<sup>83</sup> *Id* 22; Council for International Organizations of Medical Sciences (2002) 45-46.

<sup>84</sup> National Health Research Ethics Council's "Payment of trial participants in South Africa: Ethical considerations for Research Ethics Committees (RECs)" (2012) 5; Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 22.

<sup>85</sup> National Health Research Ethics Council's "Payment of trial participants in South Africa: Ethical considerations for Research Ethics Committees (RECs)" 5.

<sup>86</sup> Council for International Organizations of Medical Sciences (2002). 46.

order to prevent such occurrences, it has been suggested that accompanying guardians who give permission on behalf of minors should only be compensated for travel and direct expenses, and not for time and inconvenience.<sup>87</sup>

### **2.3.3 VULNERABLE RESEARCH GROUPS AND APPROPRIATE SUBJECT SELECTION**

As per the basic ethical guidelines, recruitment, selection, exclusion and inclusion of participants for research must be just and fair. Research participants should not be unfairly excluded or targeted on the basis of any of the prohibited grounds for discrimination such as: race, ethnicity, gender, sexual orientation, age, religious beliefs or culture, disability, level of education, and language.<sup>88</sup> Furthermore, the selection process should be in line with sound scientific aims and objectives, as outlined in the respective research protocol.<sup>89</sup>

Vulnerable population groups are individuals or collectives that: are at increased risk of research-related harm; are limited in their freedom to make choices; or are relatively incapable of protecting their own interests (ie they may be intellectually or cognitively impaired, or lack education and communication skills).<sup>90</sup> Social factors such as a lack of access to health care and poverty may also contribute the vulnerability of certain populations.<sup>91</sup>

RECs require special justification if such groups are included in a research study, and special attention should be taken to protect the rights and best interests of these subjects.<sup>92</sup>

Vulnerable research groups can be broadly categorised as follows:<sup>93</sup>

- Minors (children and adolescents)
- Pregnant Women
- Institutionalised individuals and the elderly
- Offenders

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<sup>87</sup> *Ibid.*

<sup>88</sup> Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 16.

<sup>89</sup> Moodley (2011) 329.

<sup>90</sup> Government Notice R719 "Regulations Relating to Research with Human Participants" published in published in Government Gazette 38000 dated 19 September 2014.

<sup>91</sup> Coleman *et al* (2009) 21.

<sup>92</sup> Department of Health "South African Good Clinical Practice Guidelines Second Edition" 16; Council for International Organizations of Medical Sciences (2002). 64-66.

<sup>93</sup> Department of Health "South African Good Clinical Practice Guidelines Second Edition" 16; Moodley (2011) 330.

- People with mental or behavioural disorders, not capable of giving adequate informed consent
- Persons in Dependant Relationships or Comparable Situations
- Vulnerable Communities

According to Government notice R719 “Regulations Relating to Research with Human Participants”, research involving vulnerable research groups must:

- “• involve vulnerable persons only when non-vulnerable persons are not appropriate for inclusion;
- not systematically avoid inclusion of vulnerable participants because to do so is unfairly discriminatory and vulnerable persons are potential beneficiaries of relevant research;
- be responsive to the health needs and the priorities of vulnerable persons;
- receive special attention in ethical review to ensure that research-related risks are assessed and minimized and that appropriate consent procedures are followed.”<sup>94</sup>

### **2.3.3.1 Minors (children and adolescents)**

According to Section 17 of the Children’s Act 38 of 2005, a child is defined as a person under the age of 18 years. Of particular importance when exploring the theme of research on minors are the definitions ‘therapeutic’ and ‘non-therapeutic’ research. ‘Therapeutic research’ is defined as research that holds out the prospect of direct benefit to the participant; ‘non-therapeutic’ research on the other hand means research that does not hold out the prospect of direct benefit to the participant but holds out the prospect of generalizable knowledge.<sup>95</sup> As per of Section 71(3)(a)(ii) and Section 92(a) of the NHA, research protocols involving non-therapeutic research on minors must have ministerial consent or consent from an authority delegated by the minister.<sup>96</sup> Registered RECs that have been granted permission to exercise the minister’s delegated power to approve non-therapeutic research involving children must ensure that their deliberations on

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<sup>94</sup> Government Notice R719 “Regulations Relating to Research with Human Participants” published in published in Government Gazette 38000 dated 19 September 2014.

<sup>95</sup> *Ibid.*

<sup>96</sup> S 71 and S 92 of the National Health Act 61 of 2003.



these components are properly recorded as required by the Regulations.<sup>97</sup>

The general rule is that minors should only participate in research when their participation is indispensable.<sup>98</sup> Furthermore, such research should investigate a problem that is relevant to children, and children should not be subjected to research if the research might be equally informative if it were carried out on adults.<sup>99</sup>

For minimal risk research of a sensitive nature (ie research about sexual activities or substance abuse, and so on) it may be ethically justifiable for minors over the age of 16 to consent to such research independently without parental assistance.

### **2.3.3.2 Pregnant Women**

If pregnant women are included in research studies, RECs must ensure that the participant and the foetus are not placed at unnecessary risk. Reasons for excluding women should be justifiable and scientifically sound, as researchers are ethically obliged to conduct research that does not promote gender discrimination.<sup>100</sup> Section 2.3.2 of “The South African Good Clinical Practice Guidelines” of 2006 outlines detailed conditions under which research can be conducted on pregnant women and foetuses (table 2).<sup>101</sup>

### **2.3.3.3 Institutionalised individuals and the elderly**

The elderly are also considered to be a vulnerable research group. They may be institutionalised, or develop varying levels of dementia as they get older.<sup>102</sup> When such vulnerability defining attributes are detected, RECs should take special precautions in order to protect such individuals.<sup>103</sup>

### **2.3.3.4 Offenders**

Offenders are considered to be a vulnerable population group, due to the potential impact of their incarceration on their ability to make

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<sup>97</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 30.

<sup>98</sup> Department of Health “South African Good Clinical Practice Guidelines Second Edition” 17.

<sup>99</sup> *Ibid.*

<sup>100</sup> *Ibid.* 18-20.

<sup>101</sup> *Ibid.*

<sup>102</sup> Council for International Organizations of Medical Sciences (2002). 65.

<sup>103</sup> *Ibid.*

voluntary decisions to participate in research.<sup>104</sup> Researchers should guard against coercion and undue influence when offenders are recruited and during the informed consent process.<sup>105</sup> Furthermore, a correctional service representative with relevant experience and knowledge of working with offenders should serve on the RECs when research protocols involving offenders are reviewed.<sup>106</sup>

### **2.3.3.5 People with mental or behavioural disorders, not capable of giving adequate informed consent**

When conducting research on adults incapable of giving adequate informed consent neither the NHA nor the Mental Health Care Act 17 of 2002 (MHCA) allows for proxy decision making, unless the proxy is a court appointed curator.<sup>107</sup> These Acts do however allow proxy decision making for medical treatment purposes. According to the NHA, legally appropriate proxies include: a spouse or partner; parent; grandparent; adult child; brother or sister; or another person authorised by law to act on the first mentioned persons' behalf.<sup>108</sup> The MHCA also states that an application for care, treatment and rehabilitation services for mental health care users incapable of making informed decisions, can only be made by a spouse or partner; next of kin; associate or a parent/guardian.<sup>109</sup> It can be argued however that it is unethical to exclude a group of people from research participation based on incapacity, therefore an ethical argument can be made for using the statutory treatment proxies to give consent for participation in research.<sup>110</sup> Section 3.2.4.4 of EPPS clearly highlights the minimum conditions for approving research involving incapacitated adults.

### **2.3.3.6 Persons in Dependant Relationships or Comparable Situations**

Using persons or groups who are in dependent or hierarchical relationships with researchers is ethically questionable.<sup>111</sup> Persons in such relationships include but is not limited to: patients and healthcare workers; persons with life-threatening diseases and their care-givers;

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<sup>104</sup> Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 39-40; Department of Health "South African Good Clinical Practice Guidelines Second Edition" 21.

<sup>105</sup> *Ibid.*

<sup>106</sup> *Ibid.*

<sup>107</sup> Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 37.

<sup>108</sup> National Health Act 61 of 2003.

<sup>109</sup> S1 and S27 of the Mental Healthcare Act 17 of 2002.

<sup>110</sup> Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 37.

<sup>111</sup> Moodley (2011) 330.

wards of the state and their guardians; older persons or persons' with disabilities and their caregivers; students and teachers; employees and employers.<sup>112</sup> Such persons may feel obliged or may be pressured into participating in research, so as not to offend their caregivers or superiors.<sup>113</sup> RECs should give special attention to such persons in order to ensure that informed consent is adequately obtained, and to ensure that their participation is completely voluntary and independent of any coercion whatsoever.

#### 2.3.4 POTENTIAL RISKS AND BENEFITS

According to the declaration of Helsinki, "medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects"<sup>114</sup>.

As a general rule, a risk benefit analysis must precede all biomedical research involving human participants. Researchers must ensure that the net expected benefits associated with the research should outweigh the anticipated risks.<sup>115</sup> The potential risks associated with research include physical harm, as well as psychological, social, legal and economic burdens.<sup>116</sup> Research that does not hold out the prospect of direct benefit to participants must be justified in relation to the expected benefits of society in general.<sup>117</sup> However, there should still be a reasonable risk to benefit ratio (ie the potential risk of harm to participants should not outweigh the benefit of the knowledge to be gained).

Whenever biomedical research involves human participation, there are always potential risks involved, RECs should therefore carefully review such research in order to ensure that measures to minimise risks are implemented, and that these risks are continuously monitored, assessed and documented by the researcher.<sup>118</sup>

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<sup>112</sup> Government Notice R719 "Regulations Relating to Research with Human Participants" published in published in Government Gazette 38000 dated 19 September 2014; Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 38.

<sup>113</sup> Moodley (2011) 330.

<sup>114</sup> "World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects" (2013) 310, 20 *Journal of the American Medical Association*.

<sup>115</sup> Moodley (2011) 330-331.

<sup>116</sup> Coleman *et al* (2009) 30.

<sup>117</sup> Council for International Organizations of Medical Sciences (2002). 47-49; Coleman *et al* (2009) 30.

<sup>118</sup> "World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects" (2013) 310, 20.

### 2.3.5 RESPECT FOR THE RIGHTS OF PARTICIPANTS (PRIVACY AND CONFIDENTIALITY)

The rights of research participants are not limited to informed consent only.<sup>119</sup> Participants also have a right to dignity, bodily integrity, equality, privacy and confidentiality.

There is no universally accepted definition for the term ‘privacy’ as it is context specific.<sup>120</sup> In the context of biomedical research, privacy deals with the accessibility of personal information and records of research participants.<sup>121</sup> Confidentiality, on the other hand ensures that adequate mechanisms are in place to prevent the disclosure of information that might lead to the identification of participants.<sup>122</sup> Electronic records and research data, such as completed informed consent forms, raw data, questionnaires, medical records or any potential participant identifiers must be protected and strictly access controlled.

Lately there has been a lot of discussions around privacy and confidentiality in South Africa, as the Protection of Personal Information Act 4 of 2013 (POPI) which regulates such rights is expected to commence fully in the near future. The privacy and confidentiality of research participants should therefore be protected at all costs. RECs and researchers must therefore take appropriate measures to ensure that basic standards of information protection are adhered to, both during the course of conducting research and after completion when publishing results.<sup>123</sup>

### 2.3.6 RELEVANCE AND VALIDITY OF RESEARCH

Biomedical research involving human subjects must conform to the generally accepted scientific principles, as laid out in the Declaration of Helsinki.<sup>124</sup> Moreover, it should be based on a thorough knowledge of the scientific literature and adequate and appropriate laboratory and animal experimentation.<sup>125</sup> In order for biomedical research to be

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<sup>119</sup> Moodley (2011) 332.

<sup>120</sup> Sharyl J. Nass (2009) 16.

<sup>121</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 17.

<sup>122</sup> *Ibid.*

<sup>123</sup> *Ibid.*

<sup>124</sup> “World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects” (2013) 310, 20.

<sup>125</sup> *Ibid.*

ethical, it must be scientifically valid, ie if a study is not scientifically valid all other ethical considerations become irrelevant.<sup>126</sup>

The validity of biomedical research is compromised when researchers use incorrect techniques; use the correct techniques incorrectly; selectively report results; misinterpret results; selectively cite the literature and draw unjustifiable conclusions. An important global initiative that is aimed at improving and standardizing the reporting of different types of health research, as part of a broader effort to improve the quality of research used in decision-making in healthcare is the CONSORT Statement (Consolidated Standards of Reporting Trials).<sup>127</sup> It is an evidence-based, minimum set of recommendations for reporting randomised trials.<sup>128</sup>

If the rationale and motivation for biomedical research does not ask relevant and important questions, then it is fruitless and unethical.<sup>129</sup> In order for biomedical research to be relevant, it should seek to provide the answers to important questions that significantly affect local and regional populations.<sup>130</sup> The outcomes of such research should also be translatable into mechanisms of improving the health status of such populations.<sup>131</sup>

As beautifully stated by Altman:

“We need less research, better research, and research done for the right reasons”<sup>132</sup>

Furthermore, researchers should have suitable academic qualifications and credentials and most importantly, the scientific and technical expertise to conduct the proposed research.<sup>133</sup> Last but not least, humanistic qualities such as empathy and compassion are also essential when research is being conducted on humans.<sup>134</sup>

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<sup>126</sup> Freedman "Scientific Value and Validity as Ethical Requirements for Research: A Proposed Explication" (1987) 9, 6 *IRB: Ethics & Human Research* 7-10.

<sup>127</sup> The CONSORT Group "The CONSORT Statement" (2010) Available online: <http://www.consort-statement.org/consort-2010> [Accessed 02/08/2016].

<sup>128</sup> *Ibid.*

<sup>129</sup> Department of Health "South African Good Clinical Practice Guidelines Second Edition" 9.

<sup>130</sup> *Ibid.*

<sup>131</sup> *Ibid.*

<sup>132</sup> Altman (1994) 308 *British Medical Journal* 283-284.

<sup>133</sup> Department of Health "Ethics in Health Research: Principles, Processes and Structures, Second Edition" 17; "World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects" (2013) 310, 20.

<sup>134</sup> Department of Health "South African Good Clinical Practice Guidelines Second Edition" 9-10.

## 2.4 THE ROLE OF RESEARCH ETHICS COMMITTEES (RECS)

Section 73 (1) of the NHA makes it a legal requirement that every institution, health agency and health establishment at which health research is conducted, establish or have access to a research ethics committee (REC), which is registered with the National Health Research Ethics Council (NHREC).<sup>135</sup> According to the NHREC website, there are currently 44 RECs registered in South Africa.<sup>136</sup> Any research conducted on or relating to humans in the country must be approved by a NHREC registered REC. Many South African RECs are also registered with the United States Office of Human Research Protections (OHRP). If the OHRP grants a REC Federal Wide Assurance (FWA), then collaborative research studies approved by such RECs are eligible to receive United States Federal research funding.

The more specific roles and responsibilities of RECs are mentioned throughout this dissertation, in the various sections. However, according to S 73 of the NHA the core functions of RECs are to:

- “(a) review research proposals and protocols in order to ensure that research conducted by the relevant institution, agency or establishment will promote health, contribute to the prevention of communicable or non-communicable diseases or disability or result in cures for communicable or non-communicable diseases; and
- (b) grant approval for research by the relevant institution, agency or establishment in instances where research proposals and protocol meet the ethical standards of that health research ethics committee.”<sup>137</sup>

Thus, in performing its duty, RECs protect the rights and welfare of research participants while ensuring that biomedical research is scientifically valid, relevant and ethical. RECs should be comprised of members with appropriate qualifications and experience in as many disciplines, sectors and professions as possible (within its ambit of research).<sup>138</sup> If a REC lacks the scientific expertise to review a specific research protocol, then a separate scientific review should be conducted, thereafter the protocol can be re-submitted to the REC for ethical review.<sup>139</sup>

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<sup>135</sup> National Health Act 61 of 2003.

<sup>136</sup> National Health Research Ethics Council website Available online: <http://www.nhrec.org.za/> [Accessed 25/07/2016].

<sup>137</sup> National Health Act 61 of 2003.

<sup>138</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 58.

<sup>139</sup> “The ethics of research related to healthcare in developing countries: a follow-up Discussion Paper” (2005) Nuffield Council on Bioethics 48.

Of vital importance is the field of research ethics, as the committee should be able to review and evaluate not only the science and health aspects, but also the ethics of the proposed research.<sup>140</sup> Adequate training of committee members in the field of research ethics is critical, especially for RECs that review high risk research. One local initiative aimed at training and mentoring researchers, is the “Advanced Research Ethics Training in South Africa” (ARESA) which was established in 2012.<sup>141</sup> The ARESA programme offers a postgraduate diploma in health research ethics and hosts an annual seminar aimed at enhancing networking and information exchange among members of RECs in southern Africa.<sup>142</sup> It is also essential for REC members to undergo refresher courses/training at least once during a term of office.<sup>143</sup>

Membership of RECs should also be ethnically and culturally diverse with appropriate gender representation.<sup>144</sup> Furthermore, it should not include only senior ranking officials; and it should include a lay person, preferably from the community in which research is conducted.<sup>145</sup>

Lastly, every REC must have Terms of Reference (ToR) and Standard Operating Procedures (SOPs) policies.<sup>146</sup> SOPs should describe in detail “standardised best practices for health research; compliance with national and international ethical and regulatory requirements; consistent processes about ethical issues in health research; and declarations regarding confidentiality and conflict of interest”<sup>147</sup>. The ToR should set out the formal character of the REC as well as both statutory and institutional requirements.<sup>148</sup> SOP and ToR policies, however, should not be static and should be reviewed, revised and updated on a regular basis.<sup>149</sup>

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<sup>140</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 58.

<sup>141</sup> Moodley & Rennie “Advancing research ethics training in Southern Africa (ARESA)” (2012) 4, 2 *The South African Journal of Bioethics and Law* 1-6.

<sup>142</sup> *Ibid.*

<sup>143</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 58.

<sup>144</sup> *Ibid*; Dhai & Cleaton-Jones (2011) 171-172.

<sup>145</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition”; Dhai & Cleaton-Jones (2011) 171-172.

<sup>146</sup> Department of Health “Ethics in Health Research: Principles, Processes and Structures, Second Edition” 57.

<sup>147</sup> *Id* 60.

<sup>148</sup> *Id* 57.

<sup>149</sup> *Id* 60.

## 2.5 WHAT HAPPENS AFTER RESEARCH IS COMPLETED?

Biomedical researchers and sponsors are ethically obliged to timeously disseminate research results, regardless of whether the outcomes are positive or negative.<sup>150</sup> If research is not published, it cannot contribute to generalisable knowledge.<sup>151</sup> These results may be published in various local and international journals; discussed at national and international conferences; disseminated to the public via the media; or used to build up the knowledge base in a particular field of study.

## 2.6 CONCLUDING REMARKS

Any material failure to comply with statutes, regulations; guidelines and policies relating to research on humans may constitute research misconduct, and a thorough investigation should be conducted. Such transgressions as discussed in this chapter include: conducting research without REC clearance; failure to obtain adequate informed consent; inadequate risk-benefit analysis; unfair subject selection/recruitment; coercion/exploitation of vulnerable research groups; violating the rights of participants; and any unjustifiable deviations from accepted ethical standards.

Punishment for medical researchers found guilty of misconduct may include: dismissal from employment; discontinuation of research funds; suspension or withdrawal of professional licences; a fine and in extreme cases imprisonment.<sup>152</sup>

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<sup>150</sup> Department of Health "South African Good Clinical Practice Guidelines Second Edition" 37.

<sup>151</sup> Moodley (2011) 332.

<sup>152</sup> Dhai & McQuoid-Mason (2011) 179.



## CHAPTER 3: RESEARCH MISCONDUCT AND PUBLICATION ETHICS

### 3.1 INTRODUCTION

Research misconduct is a global problem that tarnishes the reputation of researchers and research institutions and inevitably compromises the independence, integrity and credibility of the scientific record.<sup>153</sup> Studies on the prevalence of research misconduct in the developing world, particularly in Africa are scarce.<sup>154</sup> In a recent study conducted among researchers in a developing African country, 68.9% of the respondents admitted to having committed some form of scientific misconduct.<sup>155</sup>

When critically analysing the theme of 'research misconduct', one should immediately think of the other end of the spectrum, ie 'research integrity'. In order to curb the incidences research misconduct, we need to foster a culture of research integrity. Research integrity, however, does not only involve adhering to ethical rules and regulations.<sup>156</sup> Programmes aimed at developing self-reflective, critical scientists that are able and willing to take responsibility for their actions are essential in promoting a sustainable culture of scientific integrity.<sup>157</sup>

At the 2<sup>nd</sup> World conference on Research Integrity held in Singapore in 2010, the "Singapore statement on Research Integrity" was adopted. The statement is the culmination of the collective effort and insights of 340 individuals from 51 countries including: researchers, funders, representatives from universities and research institutes, and research publishers.<sup>158</sup> The purpose of this document is "to challenge governments, organizations and researchers to develop more comprehensive standards, codes and policies to promote research integrity both locally and on a global basis"<sup>159</sup>.

Core values such as accountability, honesty and trustworthiness are indispensable when conducting, writing up, and publishing research.

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<sup>153</sup> Okonta & Rossouw (2014) 15 *BMC medical ethics* 25.

<sup>154</sup> Ana *et al* (2013) 10, 3 *PLoS Med* 1-5; Okonta & Rossouw (2014) 15 *BMC medical ethics* 25.

<sup>155</sup> Okonta & Rossouw "Prevalence of scientific misconduct among a group of researchers in Nigeria" (2013) 13, 3 *Developing world bioethics* 149-157.

<sup>156</sup> Coughlin *et al* "Ethics and Scientific Integrity in Public Health, Epidemiological and Clinical Research" (2012) 34, 1 *Public Health Reviews* 71-83.

<sup>157</sup> *Ibid.*

<sup>158</sup> 2nd World Conference on Research Integrity web page "Singapore Statement on Research Integrity" (2010) Available online: <http://www.singaporestatement.org/> [Accessed 08/08/2016].

<sup>159</sup> *Ibid.*

According to the Singapore statement, the four basic principles fundamental to research integrity are: “Honesty in all aspects of research; Accountability in the conduct of research; Professional courtesy and fairness in working with others; and Good stewardship of research on behalf of others”<sup>160</sup> (figure 1). This document further highlights the fundamental professional responsibilities that researchers should adhere to, when conducting and publishing research.

As mentioned earlier, research behaviour can be broadly categorised as: deliberate misconduct often defined as fabrication, falsification, and plagiarism (FFP); questionable research practices (QRP); and responsible conduct of research (RCR).<sup>161</sup> Deliberate fabrication or falsification of data undoubtedly constitutes gross scientific misconduct.

As proposed by Dhai, deliberate misconduct should not be limited to FFP, and should also include:<sup>162</sup>

- Undeclared conflicts of interests;
- Falsification of credentials and duplicating of publications;
- Inaccurate author representation and Ghost Authorship<sup>163</sup>;
- Deviation from or failure to adhere to proposed protocol without proper permission;
- Deception in research protocols;
- Deception in carrying out of research;
- Conducting research without REC clearance;
- Failure to obtain informed consent and breach of confidentiality;
- Unjustifiable deviations from accepted ethical standards

QRPs, on the other hand, have been described as activities that ‘may be detrimental to the research process’ or that ‘do not directly damage the integrity of the research process’.<sup>164</sup> QRPs include, but are not limited to: Misrepresentation (ie publishing results of the same experiment into several partial publications, with the intention of increasing the number of publications); Inaccuracy (ie improper use of

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<sup>160</sup> 2nd World Conference on Research Integrity web page "Singapore Statement on Research Integrity" (2010).

<sup>161</sup> Mitcham (2003) 9, 2 *Science and Engineering Ethics* 273-290; Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74; Galland (2010) *2nd World Conference on Research Integrity* Singapore; Steneck (2005) *International Bioethics Conference*, Poland.

<sup>162</sup> Adapted from: Dhai, 'Preventing Research Misconduct: Some Programs in Africa', *2nd World Conference on Research Integrity* Singapore.

<sup>163</sup> Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>164</sup> *Ibid.*

statistics and data analysis, careless citational errors, and inadequate abstract or summary writing); and lastly Conflicts of Interest and Bias (ie “making decisions or presenting evidence for other than scientific or scholarly reasons”<sup>165</sup>).<sup>166</sup> According to Angell, in the US alone QRPs relating to drug trials, particularly the use of: inappropriate controls and treatment periods; improper subject selection; improper administration of competing agents and the selective publication of data to support desired conclusions wastes hundreds of millions of dollars and adversely impacts public health.<sup>167</sup> RCR is the ideal standard of research that all institutions and researchers should strive to meet, deliberate misconduct should be avoided at all costs and QRP fall somewhere between the two extremes.<sup>168</sup>

Honest error, honest difference in opinion, and errors in interpretation does not constitute research misconduct.<sup>169</sup> Researchers are still human beings after all, and are capable of making mistakes such as research design errors, calibration errors, logging errors, data entry errors etc.<sup>170</sup>

The Committee on Publication Ethics (COPE) is an internationally renowned organization that provides resources to editors and publishers on all aspects of publication ethics and, in particular on how to handle cases of research and publication misconduct.<sup>171</sup> It is the opinion of the author of this paper that every researcher and journal editor should familiarise themselves with COPEs code of conduct, and other resources available on their website (table 3).

In this Chapter, we will briefly discuss fabrication, falsification and plagiarism, and well as some of the questionable research practices, in an attempt to clarify any misconceptions that may exist.

## 3.2 FABRICATION AND FALSIFICATION

Fabrication is defined as making up data or results and recording or reporting them with the deliberate intention of deceiving the scientific

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<sup>165</sup> *Ibid.*

<sup>166</sup> *Ibid.*

<sup>167</sup> Angell (2005) "The truth about the drug companies: How they deceive us and what to do about it" as cited in Steneck (2006).

<sup>168</sup> Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>169</sup> "Guidelines for Good Practice in the Health Care Professions: General Ethical Guidelines for Health Researchers" (2008) Health Professions Council of South Africa 9; Air University website "Scientific Ethics" (2002) Available online: <http://www.au.af.mil/au/awc/awcgate/doe/benchmark/ch16.pdf> [Accessed 24/08/16].

<sup>170</sup> Air University website "Scientific Ethics" (2002).

<sup>171</sup> Committee on Publication Ethics website (2016) Available online: <http://publicationethics.org/about> [Accessed 25/05/2016].

community.<sup>172</sup> These fabricated results or data are then used to publish papers in scientific journals; are presented at local and international scientific gatherings or conferences; or used to obtain patents and grants.<sup>173</sup>

Falsification includes fabrication, and is defined as “manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record”<sup>174</sup> (ie the intentional suppression, distortion or manipulation of true scientific findings obtained from experimental or observational studies results, without any sound scientific or statistical justification).<sup>175</sup>

Other forms of fabrication and falsification include: the intentional manipulation of data or results in order to make it fit a desired hypothesis; selective reporting of results; failing to report results or findings that conflict current reports in the literature; and manipulating an image with the intention of obscuring or eliminating information.<sup>176</sup>

A high profile case of research misconduct in South Africa that involved fabrication and falsification of data is that of Werner Bezwoda. Dr Bezwoda is an oncologist in private practice, who at the time worked part-time at the University of Witwatersrand. In the 1990s he conducted research involving the use of high-dose chemotherapy and autologous stem cell transplantation in patients with advanced breast cancer.<sup>177</sup> His research attracted a lot of attention both locally and internationally, as it was the only study of its kind that showed beneficial effects with such radical treatment.<sup>178</sup> In 1999 he presented his research at the annual meeting of the American Society of Clinical Oncology and at the European Cancer Conference.<sup>179</sup> By 2001, one of Bezwoda’s published papers on high-dose chemotherapy treatment regimens had already been cited over 300 times.<sup>180</sup>

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<sup>172</sup> Khanyile *et al* (2006) 29, 1 *Curationis* 40-45; Office of Research Integrity website (2016) Available online: <http://ori.hhs.gov> [Accessed 15/02/2016].

<sup>173</sup> Coughlin *et al* (2012) 34, 1 *Public Health Reviews* 71-83.

<sup>174</sup> Office of Research Integrity website (2016).

<sup>175</sup> Coughlin *et al* (2012) 34, 1 *Public Health Reviews* 71-83; Fanelli "How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data" (2009) 4, 5 *PloS one* e5738.

<sup>176</sup> Khanyile *et al* (2006) 29, 1 *Curationis* 40-45; World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016) Available online: <http://www.wame.org/about/recommendations-on-publication-ethics-policies#Plagiarism> [Accessed 24/08/2016].

<sup>177</sup> Moodley (2011) 333.

<sup>178</sup> *Ibid.*

<sup>179</sup> Weiss *et al* "High-dose chemotherapy for high-risk primary breast cancer: an on-site review of the Bezwoda study" (2000) 355, 9208 *The Lancet* 999-1003.

<sup>180</sup> Moodley (2011) 333.

In 2000, a team of US oncologists conducted an on-site review in order to verify Bezwoda's data, as they were preparing to conduct a larger randomised trial aimed at confirming Bezwoda's results.<sup>181</sup> The on-site review revealed discrepancies between the records reviewed and the data he presented; and the University's REC had no record of approval for his study.<sup>182</sup> Moreover, questions were also raised as to whether participants were aware that they were participating in a clinical trial, as no form of informed consent was found.<sup>183</sup> Bezwoda eventually admitted that the protocol for one of his studies was written long after the study was completed.<sup>184</sup> Furthermore, he admitted to using a different control chemotherapy regimen from that described in presented data.<sup>185</sup>

In March 2000, at a University disciplinary hearing Dr Bezwoda was found guilty of research misconduct and dismissed.<sup>186</sup> In August 2003, the HPCSA also suspended his physician's license for a period of five years.<sup>187</sup>

The intentional publication of fabricated and falsified results undermines the reliability and the integrity of the research record.<sup>188</sup> The culture of scientific research is based on integrity and trust. If the unscrupulous practices of fabrication and falsification are not managed with the greatest of urgency, more and more of these bogus studies will be cited, and like a malignancy, its prevarication will rapidly corrupt and metastasise throughout the scientific literature.

### 3.3 PLAGIARISM

There are many overlapping definitions of plagiarism. The most popular and accepted being that of the ORI. However, the author of this paper suggests combining the ORI definition with that from the World Association of Medical Editors (WAME), thus defining plagiarism as:

"The use of another person's published or unpublished ideas, processes, results, words (or other intellectual property including those obtained through confidential review research proposals and

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<sup>181</sup> Weiss *et al* (2000) 355, 9208 *The Lancet* 999-1003.

<sup>182</sup> *Ibid.*

<sup>183</sup> *Ibid.*

<sup>184</sup> Moodley (2011) 333; Weiss *et al* (2000) 355, 9208 *The Lancet* 999-1003.

<sup>185</sup> Moodley (2011) 333; Weiss *et al* (2000) 355, 9208 *The Lancet* 999-1003.

<sup>186</sup> Rettig *et al* (2007) "False Hope: Bone Marrow Transplantation for Breast Cancer" 246-247.

<sup>187</sup> *Ibid.*

<sup>188</sup> Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

manuscripts) without attribution or permission, and presenting them as new and original.”<sup>189</sup>

So called ‘borrowed’ information is not just limited to written texts (articles, books, dissertations, theses), but also includes audio-visual sources such as presentations; multimedia sources such as videos; internet sources such as websites; spoken text such as speeches and lectures; as well as ideas private research methods, or any other form of privileged communication.<sup>190</sup>

Every academic institution must have strict plagiarism policies in place, and every researcher affiliated with such institutions should be made aware of such policies, and the processes that will be followed should a researcher be found guilty of plagiarism. Before embarking on any sort research activity, prospective researchers usually attend research methodology courses where topics like plagiarism and appropriate referencing are discussed at great length.

Another complicated and controversial form of plagiarism is self-plagiarism. Self-plagiarism is when an author republishes work in its entirety or reuses portions of previously published work or data on the same topic in another publication without proper acknowledgment.<sup>191</sup> *Prima facie* ‘self-plagiarism’ is indeed an oxymoron as one could ask the question “How can one steal from oneself?”<sup>192</sup>. There are, however, complex issues at play, including copyright law; how much text re-use is permissible; when to reference; as well as the appropriate use of quotation marks.<sup>193</sup> Self-plagiarism can be broadly categorised into: redundant or duplicate publications; academic self-plagiarism; ‘salami slicing’; and text recycling.<sup>194</sup>

Academic self-plagiarism or ‘double-dipping’ occurs when a student submits an entire dissertation or theses (or a substantial part of this work) to fulfil a course or degree requirement, even though that paper had earlier been submitted to satisfy the requirements for another programme at a different university or academic institute.<sup>195</sup> ‘Salami

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<sup>189</sup> World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016); Office of Research Integrity website (2016).

<sup>190</sup> Moodley (2011) 334-335; Coughlin *et al* (2012) 34, 1 *Public Health Reviews* 71-83.

<sup>191</sup> World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016); The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)" Available online: [http://ori.hhs.gov/education/products/columbia\\_wbt/rcr\\_conflicts/foundation/index.html](http://ori.hhs.gov/education/products/columbia_wbt/rcr_conflicts/foundation/index.html) [Accessed 28/08/2016].

<sup>192</sup> Woker "Oops I said it again... self-plagiarism or text re-use: when or is it acceptable?" (2011) 32, 2 *Obiter* 233-248.

<sup>193</sup> *Ibid.*

<sup>194</sup> Roig "Avoiding plagiarism, self-plagiarism, and other questionable writing practices: A guide to ethical writing" (2011) 16; Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>195</sup> Roig (2011) 19.

slicing’, on the other hand, refers to the segmenting of a large study into two or more publications.<sup>196</sup> This practice is unacceptable as it may lead readers to believe that data presented in each publication (‘salami slice’) is derived from a different subject sample.<sup>197</sup> Text recycling is defined as an author’s “reuse of portions of text that have appeared previously in other works”.<sup>198</sup> This practice is problematic and difficult to regulate, as official published guidelines relating to ‘how much text recycling is permissible’ are scarce.<sup>199</sup>

Plagiarism may not have a significant impact on the reliability of the research record (provided that the original work being plagiarised is scientifically accurate).<sup>200</sup> It does, however, result in wasted funds used for reviewing and publishing of plagiarised work, and furthermore it undermines trust and collegiality within the scientific community.<sup>201</sup> There are various software packages on the market that are able to detect plagiarism, such as Turnitin®<sup>202</sup> and Dejavu®<sup>203</sup>. Such programmes are used routinely by institutes of higher learning to screen academic papers, dissertations and theses for similarity.

An excellent paper written by Miguel Roig, titled “Avoiding plagiarism, self-plagiarism, and other questionable writing practices: A guide to ethical writing” is readily available online. It highlights 27 comprehensive guidelines dealing with plagiarism, self-plagiarism and ethical scientific writing. It is a must read for every researcher both novice and experienced. This paper as well as other important international policies and guidelines dealing with good publication practices are listed in table 3.

### 3.4 INAPPROPRIATE AUTHORSHIP

Biomedical research is often complex and requires the expertise of a research team. Furthermore, technological advances have allowed researchers from all around the world to work on collaborative studies which invariably result in multi-authored publications.<sup>204</sup> There is no universal definition for ‘authorship’, however according to the WAME, in order for a researcher to qualify for authorship, he/she should make a

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<sup>196</sup> *Ibid.*

<sup>197</sup> *Ibid.*

<sup>198</sup> *Ibid.*

<sup>199</sup> *Ibid.*

<sup>200</sup> Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>201</sup> *Ibid.*

<sup>202</sup> Turnitin 2101 Webster St., Suite 1800, Oakland, California, 94612.

<sup>203</sup> A project by artwarez.org © TPPSTDNK.

<sup>204</sup> Roig (2011) 35.

significant intellectual contribution to a study (ie contribute to writing the manuscript, as well as reviewing the final draft).<sup>205</sup>

Questions regarding authorship that often arise include: Who should be an author and in what sequence?; Should people in power such as heads of departments receive automatic authorship?; and Who should receive acknowledgement? Such matters should be resolved early in the research process, so as to avoid any disputes which may delay the publishing of a paper.<sup>206</sup> A number of professional societies and many scientific journals have published guidelines relating to authorship.

The guidelines of the International Committee of Medical Journal Editors (ICMJE) are by far the most popular, and have been adopted by approximately 3000 scientific journals worldwide.<sup>207</sup> According to the ICMJE, an individual only qualifies for authorship if he/she satisfies all of the following criteria:

“Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

Drafting the work or revising it critically for important intellectual content; AND

Final approval of the version to be published; AND

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.”<sup>208</sup>

Furthermore, an author should be able to identify which co-authors are responsible for different parts of the work.<sup>209</sup> Individuals who do not meet all of the criteria mentioned above, should not be listed as authors, but rather acknowledged.<sup>210</sup>

Other popular terms coined under the ambit of inappropriate authorship include, ‘Ghost Authorship’ and ‘Honorary’ or ‘Gift’ authorship. A ghost author is an individual who has made a substantial contribution to a work, but is not named as an author.<sup>211</sup> This practice has become

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<sup>205</sup> World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016).

<sup>206</sup> *Ibid.*

<sup>207</sup> A list of journals following the ICMJE recommendations is available online at: <http://www.icmje.org/journals-following-the-icmje-recommendations/>.

<sup>208</sup> International Committee of Medical Journal Editors "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (2015) 2.

<sup>209</sup> *Ibid.*

<sup>210</sup> *Ibid.*

<sup>211</sup> Wislar *et al* "Honorary and ghost authorship in high impact biomedical journals: a cross sectional survey" (2011) 343 *BMJ* d6128; Mercola.com website "How Big Pharma Fools Even Your Doctor" (2011) Available online: <http://articles.mercola.com/sites/articles/archive/2011/11/26/medical-journals-using-ghost-writers.aspx> [Accessed 28/08/16].



increasingly popular in the pharmaceutical and biomedical device industries where medical writers are paid large sums of money to write journal articles detailing results of clinical trials, but are not credited with authorship or acknowledgement.<sup>212</sup> It has been reported that these ghost writers are paid substantial amounts of money by companies in order to ensure these articles are written in way that portrays their product in a favourable light.<sup>213</sup> Thereafter, these companies recruit well-known academics and expert researchers in the field to write a 'balanced' review of their product.<sup>214</sup> In order to facilitate the write-up, these academics are then furnished with a draft paper already written to specification by the ghost author.<sup>215</sup> Using well-known academics supposedly improves the 'credibility' of these papers, and consequently streamlines peer-review and publication.<sup>216</sup>

Honorary or gift authorship basically entails including an individual who does not meet the authorship criteria highlighted above, as an author.<sup>217</sup> This practice is common in academe, where junior staff members are coerced into including heads of departments and senior consultants as co-authors in their publications. The pressures of publishing, receiving funding, promotions and gaining respect from peers, further exacerbate this practice.<sup>218</sup>

As part of the drive to preserve the credibility and integrity of the scientific record, researchers; academic and research institutes; and scientific journals should encourage authors to adhere to currently accepted criteria for authorship. Journal editors should also be wary of the unethical, bias phenomenon of 'Ghost writing'.

### 3.5 CONFLICTS OF INTEREST AND BIAS

A conflict of interest arises when an individual's relationship to an organisation/industry or other party has the potential to compromise or bias professional judgement or objectivity in the conduct of scholarly or scientific research.<sup>219</sup> According to the ORI, "A conflict of interest

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<sup>212</sup> Coughlin *et al* (2012) 34, 1 *Public Health Reviews* 71-83; Roig (2011) 39.

<sup>213</sup> Mercola.com website "How Big Pharma Fools Even Your Doctor" (2011) Available online: <http://articles.mercola.com/sites/articles/archive/2011/11/26/medical-journals-using-ghost-writers.aspx> [Accessed 28/08/2016].

<sup>214</sup> Mercola.com website "How Big Pharma Fools Even Your Doctor" (2011).

<sup>215</sup> Mercola.com website "How Big Pharma Fools Even Your Doctor" (2011); Roig (2011) 39.

<sup>216</sup> Mercola.com website "How Big Pharma Fools Even Your Doctor" (2011).

<sup>217</sup> Roig (2011) 37.

<sup>218</sup> The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)"; Korn "Conflicts of interest in biomedical research" (2000) 284, 17 *JAMA* 2234-2237.

<sup>219</sup> The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)"; Roig (2011) 40.

implies only the potential for bias not a likelihood”<sup>220</sup>. According to Steneck, bias means “making decisions or presenting evidence for other than scientific or scholarly reasons”<sup>221</sup>. The basis of scientific research is objectivity and the moment objectivity is clouded by bias, then research is compromised.

Conflicts of interest can be broadly categorised as either tangible or intangible.<sup>222</sup> Intangible conflicts of interest are often overlooked and includes *inter alia*, conflicts of interest at an individual level; intellectual bias; and conflicts of conscience.<sup>223</sup> Conflicts of interest at an individual level relate to the pressures of publishing, securing funding, academic promotions and gaining respect from peers.<sup>224</sup> Such pressures may lead to diminished objectivity, thus resulting in bias.<sup>225</sup> Intellectual bias includes, but is not limited to, unethical peer-review.<sup>226</sup> Conflicts of conscience occur when a personal belief influences objectivity in research, for example personal or religious views may cloud a researcher’s objectivity on a study involving abortion.<sup>227</sup>

Tangible or measurable conflicts of interest mainly involve financial gain or benefit.<sup>228</sup> The concept of financial conflict of interest is beautifully summarised in this statement by Johnston:

“Traditionally, academic biomedical research institutions and for-profit companies have had different missions. Academic institutions have focused on teaching, research, and public service, whereas companies have focused on generating revenue through commercial activities. But the distinction between their missions is becoming blurred now that academic institutions and their employees have opportunities to make significant amounts of money—from research contracts, equity holdings, patents, and other relationships with industry, particularly pharmaceutical and biotechnology companies.”<sup>229</sup>

When researchers or research institutions receive significant monetary reward from industry for conducting research (in particular when a company/industry has vested interest in the outcomes of such research) or have a financial stake in their own research, then there is

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<sup>220</sup> The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)".

<sup>221</sup> Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>222</sup> The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)"

<sup>223</sup> *Ibid.*

<sup>224</sup> *Ibid.*; Korn (2000) 284, 17 *JAMA* 2234-2237.

<sup>225</sup> The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)".

<sup>226</sup> *Ibid.*

<sup>227</sup> *Ibid.*

<sup>228</sup> *Ibid.*

<sup>229</sup> Johnston (2008) "Conflict of Interest in Biomedical research in From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns" 31.

always a risk of compromised or obscured objectivity and bias.<sup>230</sup> This in turn, may affect the quality of biomedical research which may result in the harming of research subjects, patients or anyone who relies on the research.<sup>231</sup> Financial conflicts of interest include but are not limited to: having received fees for consulting; having received research funding; having been employed by a related company; holding stocks or shares in a company which might be affected by the publication of a paper; and having received funds reimbursed for traveling to /attending a related symposia, or talk.<sup>232</sup>

Several American professional societies and scientific journals have adopted a 'zero tolerance' policy when dealing financial conflicts of interest (ie "all investigators and team members directly responsible for patient selection, the informed consent process and/or clinical management in a trial must not have equity, stock options or comparable arrangement in companies sponsoring a trial"<sup>233</sup>), while others have set very high thresholds.<sup>234</sup> The impact and extent of financial conflict of interest on biomedical research have been spotlighted by various studies that show, a strong correlation between positive reviews/conclusions about certain drugs and prior financial support from industries/companies linked with these drugs.<sup>235</sup>

One highly publicised case is that of Jesse Gelsinger and the University of Pennsylvania. Jesse was an American research subject enrolled in a gene therapy clinical trial, who tragically lost his life as an indirect result of 'questionable research practices'. In this particular case, one of the co-investigators Dr James M Wilson as well as the University stood to gain significant financial compensation from the success of this clinical trial.<sup>236</sup> Moreover, they had failed to adequately disclose the extent of their financial interests in the study.<sup>237</sup> It was also reported that Jesse was not informed that "several other patients had experienced serious side effects from the therapy, or that three monkeys had died of a clotting disorder and liver inflammation after

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<sup>230</sup> *Ibid.*

<sup>231</sup> *Ibid.*

<sup>232</sup> Sage publishing website "Declaration of Conflicting Interests Policy" Available online:

<https://uk.sagepub.com/en-gb/afr/declaration-of-conflicting-interests-policy> [Accessed 29/08/2016].

<sup>233</sup> As referenced in The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)".

<sup>234</sup> *Ibid*; Rockwell "Ethics of peer review: a guide for manuscript reviewers" (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 9.

<sup>235</sup> Roig (2011) 40; Johnston (2008); Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74.

<sup>236</sup> Wilson "The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research" (2010) 36, 295 *American Journal of Law & Medicine* 295.

<sup>237</sup> *Ibid*; Steneck (2006) 12, 1 *Science and Engineering Ethics* 53-74; Benbow "Conflict+(and) Interest: Financial Incentives and Informed Consent in Human Subject Research" (2003) 17, 181 *Notre Dame JL Ethics & Pub. Pol'y* 181.

being injected”.<sup>238</sup> It is alleged that due the financial conflict of interest, the research team failed to inform Jesse of the potential dangers. Thus, this conflict of interest and inadequate informed consent indirectly contributed to his death.

Non-financial conflicts of interest would include any relationship that could inappropriately influence or have the potential to influence professional judgment, such as personal relationships (eg close personal friends or immediate family members). Journal editors, and peer reviewers also need to disclose conflicts of interest, and if need be withdraw from the review and selection process for the relevant submissions.<sup>239</sup>

It is best practice to always disclose financial and non-financial conflicts of interest (be it actual or perceived). Academic and research institutes must have sound policies and guidelines in place relating to conflicts of interest, and both novice and senior researchers should be familiar with these documents. Many international professional societies have published well-formulated guidelines relating to conflicts of interest in medical research (table 3).

### 3.6 ETHICAL PEER-REVIEW

Peer-review is considered by many to be the benchmark of the scientific publication process and is critical in ensuring the dissemination of sound scientific knowledge (ie “it facilitates a fair hearing for a manuscript among members of the scientific community”<sup>240</sup>).<sup>241</sup> As stated by Rockwell, the peer-review process “provides a scientific stamp of approval to the paper and its contents”.<sup>242</sup> It is unethical to allow a flawed paper devoid of any scientific merit to pass unchallenged into the peer-reviewed literature.<sup>243</sup>

Peer-reviewers are usually experts on a particular scientific subject matter, and are usually required to have at least: a history of having

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<sup>238</sup> Sibbald "Death But One Unintended Consequence of Gene-Therapy Trial" (2001) 164, 11 *Canadian Medical Association Journal* 1612-1612.

<sup>239</sup> International Committee of Medical Journal Editors "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (2015) 4.

<sup>240</sup> International Committee of Medical Journal Editors "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (2015) 5.

<sup>241</sup> The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)"; World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016).

<sup>242</sup> Rockwell (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 12.

<sup>243</sup> *Ibid.*

conducted and published original research; formal training in the relevant science; as well as experience in previous critical appraisal of manuscripts.<sup>244</sup>

The following guiding principles should be adhered to during the peer-review process:

- Manuscripts submitted to journals, prior to publication, are privileged communications and are the intellectual property of the authors. Both editors and peer-reviewers must therefore treat manuscripts as confidential documents.<sup>245</sup> Peer-reviewers are not allowed to cite or use any data from a manuscript that they have reviewed, prior to its official publication.<sup>246</sup>
- Peer-reviewers should provide objective, unbiased, timely, accurate, clear, concise, justifiable and constructively critical reports. Furthermore, reviewers should uphold the precept of collegiality and refrain from making rude, snide, sarcastic and argumentative remarks when writing reviews.<sup>247</sup>
- Timeliness is extremely important in the peer-review process. It is unfair for a journal to accept a paper for review, if it cannot be reviewed within the specified time frame (as there is always a risk of the manuscript becoming outdated).<sup>248</sup>
- Manuscripts should be reviewed based on: their suitability for publication in a specific journal; the importance and novelty of the science; the appropriateness of the materials, methods and research design; the quality, validity and interpretation of the data; appropriate statistical analysis; as well as the reliability and validity of the conclusions drawn from the study.<sup>249</sup>

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<sup>244</sup> World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016).

<sup>245</sup> International Committee of Medical Journal Editors "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (2015) 4; Rockwell (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 10; World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016).

<sup>246</sup> Committee on Publication Ethics "Guidelines on Good Publication Practice" (1999) 44.

<sup>247</sup> Rockwell (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 16; Committee on Publication Ethics "COPE Ethical Guidelines for Peer Reviewers" (2013) Available online: [http://publicationethics.org/files/Peer%20review%20guidelines\\_0.pdf](http://publicationethics.org/files/Peer%20review%20guidelines_0.pdf) [Accessed 25/08/2016].

<sup>248</sup> Committee on Publication Ethics "COPE Ethical Guidelines for Peer Reviewers" (2013).

<sup>249</sup> Rockwell (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 13.

- Editors and reviewers should not exclude from consideration credible studies with inconclusive findings or credible studies that challenge the existing dogma.<sup>250</sup>
- Peer-reviewers should declare all real and perceived conflicts of interest and if need be recuse themselves from the peer-review process.<sup>251</sup> An academic/intellectual conflict of interest occurs when a reviewer interferes with the peer-review process for some type of intangible personal gain.<sup>252</sup> If a manuscript is 'too closely related to your own work', then there is always a risk of bias.<sup>253</sup>
- Most journals have strict policies and ethical guidelines for studies conducted on human or animal subjects.<sup>254</sup> Ensuring that a study complies with journal policies, institutional REC policies as well as national regulations and guidelines governing research on humans is an important part of the peer review process.<sup>255</sup>
- If a reviewer suspects serious breaches in publication ethics and/or research misconduct, he/she should notify the editor in confidence.<sup>256</sup> Both editors and the reviewers, however, should be thorough, thoughtful and extremely discreet in their discussions, deliberations and planned actions, as the consequences for the authors, the journal and the scientific record could be calamitous.<sup>257</sup>

### 3.7 MAINTAINING THE INTEGRITY OF THE SCIENTIFIC LITERATURE

The drive to publish or perish coupled with financial and professional incentives to conduct research, as well as the media's recent portrayal of the dangers associated with biomedical research, against the backdrop of an increase in the number of reported cases of research

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<sup>250</sup> *Ibid*; International Committee of Medical Journal Editors "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (2015) 5.

<sup>251</sup> Rockwell (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 5; International Committee of Medical Journal Editors "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (2015) 4; Committee on Publication Ethics "COPE Ethical Guidelines for Peer Reviewers" (2013).

<sup>252</sup> The Office of Research Integrity website "RCR Conflicts of Interest Module (e-Seminar)".

<sup>253</sup> *Ibid*.

<sup>254</sup> Rockwell (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 15.

<sup>255</sup> *Ibid*.

<sup>256</sup> World association of medical editors "Recommendations on Publication Ethics Policies for Medical Journals" (2016).

<sup>257</sup> Rockwell (2005) *New Have (US): Office of research integrity, US. Department of Health and Human Services* 16.

misconduct has led to increased public and regulatory scrutiny of biomedical research. This concern however is not unwarranted as there is consensus in the scientific community that the number of reported cases of research misconduct, as well as the journal retraction indices are unacceptably high.

Strategies aimed at combatting this scourge should be preventative rather than punitive or corrective in nature. Understanding the causes of, and contributing factors associated with research misconduct are essential in devising such strategies.<sup>258</sup> At the request of the US ORI, The Institute of Medicine, in collaboration with the National Research Council's Division on Earth and Life Studies, formed the Committee on Assessing Integrity in Research Environments, in 2001. Some of the committee's recommendations are listed below:

- Funding agencies should establish research grant programs to identify, measure, and assess factors that influence integrity in research.<sup>259</sup>
- Research institutions should develop and implement comprehensive programs designed to promote integrity in research, using multiple approaches adapted to the specific environments within each institution.<sup>260</sup>
- Institutions should implement effective educational programs that enhance the responsible conduct of research.<sup>261</sup>
- "Research institutions should evaluate and enhance the integrity of their research environments using a process of self-assessment and external peer review in an ongoing process that provides input for continuous quality improvement."<sup>262</sup>

As highlighted by the committee, identifying and understanding the factors that influence research integrity is the first step in preserving and restoring the integrity of the scientific record. The scientific literature is only as reliable as the trustworthiness and calibre of the research team, therefore the development and training of ethical, adequately qualified, self-reflective researchers is crucial in fighting the battle against scientific misconduct.

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<sup>258</sup> The Organisation for Economic Co-operation and Development (OECD) Global Science Forum "Best Practices for Ensuring Scientific Integrity and Preventing Misconduct" (2007) 11-13.

<sup>259</sup> National Research Council & Medicine (2002) "Integrity in Scientific Research: Creating an Environment that Promotes Responsible Conduct" 12-13.

<sup>260</sup> *Ibid.*

<sup>261</sup> *Ibid.*

<sup>262</sup> *Ibid.*

It is however unreasonable to expect the research process to be completely error free. How does one manage a situation where a fraudulent or inaccurate study manages to slip through the cracks in the system and is published in the scientific literature?

According to the COPE, journal editors should consider:

Retraction of a publication if:

- “• they have clear evidence that the findings are unreliable, either as a result of misconduct (e.g. data fabrication) or honest error (e.g. miscalculation or experimental error)
- the findings have previously been published elsewhere without proper cross-referencing, permission or justification (i.e. cases of redundant publication)
- it constitutes plagiarism
- it reports unethical research<sup>263</sup>

Issuing an expression of concern if:

- “• they receive inconclusive evidence of research or publication misconduct by the authors
- there is evidence that the findings are unreliable but the authors' institution will not investigate the case
- they believe that an investigation into alleged misconduct related to the publication either has not been, or would not be, fair and impartial or conclusive
- an investigation is underway but a judgement will not be available for a considerable time<sup>264</sup>

Issuing a correction if:

- “• a small portion of an otherwise reliable publication proves to be misleading (especially because of honest error)
- the author / contributor list is incorrect (i.e. a deserving author has been omitted or somebody who does not meet authorship criteria has been included)<sup>265</sup>

Fraudulent publications should be retracted by their author(s); however, editors may also retract publications (or issue expressions of concern) if all or some of the authors refuse to retract the publication themselves.<sup>266</sup> Once an official investigation has concluded that a

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<sup>263</sup> Committee on Publication Ethics "Retraction Guidelines" (2009) Available online: <http://publicationethics.org/files/retraction%20guidelines.pdf> [Accessed 14/09/16].

<sup>264</sup> *Ibid.*

<sup>265</sup> *Ibid.*

<sup>266</sup> *Ibid.*



journal has published a fraudulent article, editors should first ask all the authors to submit a signed retraction, declaring that they accept full responsibility for the retraction.<sup>267</sup> If one or all of the authors refuse, then the editor must write a statement to accompany the retraction or obtain and publish an official statement from the institution that the guilty authors are affiliated to.<sup>268</sup> Moreover, these research institutions should take on the responsibility of scrutinising all other publications by the guilty authors, in order to identify other possible fraudulent studies.<sup>269</sup>

Editors must also ensure that all retracted articles are clearly identified as having been retracted in all electronic sources (this should include the journal website; bibliographic databases; as well as electronic search engines) (figure 2).<sup>270</sup> As highlighted by Sox & Rennie, it is also imperative that journal editors make it mandatory for authors submitting papers to journals, to ensure that they have not cited any retracted articles in their reference lists.<sup>271</sup>

Scientists have a moral duty and a professional obligation to warn the scientific community of these tainted publications, so as to prevent contamination of the literature, through inadvertent citation of such publications.<sup>272</sup> With technological advancements, electronic journals are readily accessible on the world-wide-web, making the dissemination of scientific information available all around the world. The regulation and enforcement of ethical research however, is controlled locally.<sup>273</sup> Cleansing the medical literature of tainted publications is a complex task that requires a collective effort on the part of researchers, research institutes, scientific publishers and government institutions.

### 3.8 MANAGING ALLEGATIONS OF RESEARCH MISCONDUCT

The United States was one of the first countries in the world to establish a governmental system for evaluating allegations of scientific fraud and misconduct. In March 1989, the US congress established the Office of Scientific Integrity in the Office of the Director in the National Institutes of Health, and the Office of Scientific Integrity Review in the

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<sup>267</sup> Sox & Rennie (2006) 144, 8 *Annals of Internal Medicine* 609-613.

<sup>268</sup> *Ibid.*

<sup>269</sup> *Ibid.*

<sup>270</sup> Committee on Publication Ethics "Retraction Guidelines" (2009); Sox & Rennie (2006) 144, 8 *Annals of Internal Medicine* 609-613.

<sup>271</sup> Sox & Rennie (2006) 144, 8 *Annals of Internal Medicine* 609-613.

<sup>272</sup> *Ibid.*

<sup>273</sup> *Ibid.*

Office of the Assistant Secretary for Health (in 1992, these offices were consolidated into the Office of Research Integrity (ORI)).<sup>274</sup>

The ORI is considered by many to be an authority in promoting research integrity and managing research misconduct, and many countries, including South Africa, use their policies and guidelines as a benchmark. In 2005, the ORI published a document titled "Sample Policy and Procedures for Responding to Allegations of Research Misconduct".<sup>275</sup> The purpose of this document is to aid institutions with limited resources and/or experience to address research misconduct and to develop suitable policies and procedures.<sup>276</sup> Even though the ORI deals only with cases of misconduct relating to federally-funded research, its influence has extended informally to other privately-funded research projects, and many research and academic institutes both in the US and internationally have adopted the ORI's administrative procedures for handling research misconduct.<sup>277</sup> Furthermore, many South African Universities are involved in collaborative research that is funded by United States Public Health Service (USPHS). These institutes are legally compelled to notify the ORI of any alleged research misconduct involving USPHS funds, and to develop and implement processes for responding to such allegations that are consistent with US Federal regulations.<sup>278</sup>

In South Africa, the regulatory framework for dealing with research misconduct allegations begins at the institutional level (ie through the RECs); followed by the NHREC and its CADC; thereafter the matter may be referred to statutory professional bodies such as the HPCSA and, lastly, if need be, legal processes may be instituted.<sup>279</sup>

In compliance with Section 72 of the NHA, the South African NHREC established the CADC. As a standing committee of the NHREC, its mandate is to: adjudicate complaints relating to the functioning of RECs; to hear complaints from researchers who believe that they are

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<sup>274</sup> Office of Research Integrity website (2016).

<sup>275</sup> Office of Research Integrity

"Sample Policy & Procedures for Responding to Research Misconduct Allegations" (2005) Available online: <http://ori.hhs.gov/sample-policy-procedures-responding-research-misconduct-allegations> [Accessed 15/08/2016].

<sup>276</sup> *Ibid.*

<sup>277</sup> Sox & Rennie (2006) 144, 8 *Annals of Internal Medicine* 609-613.

<sup>278</sup> University of Cape Town Research Office "Statement on Dealing with Allegations of Research Misconduct Under United States Public Health Service (USPHS) Research-related Activities for Foreign Institutions" (2015) Available online: [http://www.researchoffice.uct.ac.za/usr/researchoffice/integrity/ori-foreign-statement\\_11-20-2015.pdf](http://www.researchoffice.uct.ac.za/usr/researchoffice/integrity/ori-foreign-statement_11-20-2015.pdf) [Accessed 21/09/2016].

<sup>279</sup> Dhaj "Best Practices For Ensuring Scientific Integrity and Preventing Misconduct – South African Processes and Procedures" Organisation for Economic Co-operation and Development website: OECD Global Science Forum 2007.

being unfairly discriminated against by RECs; to refer matters involving allegations of violation of ethical or professional rules or standards by health care providers to the relevant statutory health professional council or body; to institute remedial measures and disciplinary action where warranted; and to facilitate compliance with legal, ethical and professional norms and standards as required for responsible conduct of research.<sup>280</sup>

The CADC first published the “Guideline for the Management of Complaints” document in 2012, and later updated it in 2015 (table 2). Its content of vital importance as it outlines *inter alia*,<sup>281</sup>

- The process of completing the relevant complaint, response and appeals forms;
- The processes of pre-investigation screening and the investigation of a complaints;
- The rights of a respondent;
- The principles that need to be adhered to during the investigation;
- Possible actions that can be taken by the NHREC; and
- The Appeals process

Please see the flowchart outlining the complaints process followed by the NHREC CADC (figure 3).

The basic moral principles that should be followed when conducting a misconduct investigation include: fairness, confidentiality, integrity, and prevention of detriment.<sup>282</sup> Research misconduct investigations must therefore adhere to the highest standards of integrity, accuracy, sensitivity and fairness, as the reputations of researchers are at stake.<sup>283</sup> However, investigators must be aware that there may be occasions when a balance has to be struck in the application of these principles, eg, “it may, in certain circumstances prove to be impracticable to undertake a detailed screening of the allegations

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<sup>280</sup> Department of Health “National Health Research Ethics Committee Annual Report (2014-2015)” (2015) Department of Health website 11-12; National Health Research Ethics Council's Complaints and Advisory Disciplinary Committee "Guideline for the Management of Complaints" (2015) 2.

<sup>281</sup> National Health Research Ethics Council's Complaints and Advisory Disciplinary Committee "Guideline for the Management of Complaints" (2015) 1.

<sup>282</sup> UK Research Integrity Office "Procedure for the Investigation of Misconduct in Research" (2008) 21-26.

<sup>283</sup> The Organisation for Economic Co-operation and Development Global Science Forum "Best Practices for Ensuring Scientific Integrity and Preventing Misconduct" (2007) 11; UK Research Integrity Office "Procedure for the Investigation of Misconduct in Research" (2008) 21-26.

without releasing the complainant's identity to the respondent"<sup>284</sup>  
However, any retaliation or threat of retaliation against a complainant, should be treated as an act of research misconduct and should result in disciplinary action.<sup>285</sup>

From an administrative perspective, Lock *et al* proposed that regulations concerning scientific misconduct investigations should meet the following conditions:

- “• It should be universal, and extend across all research disciplines (not only clinical research)
- These regulations must be promulgated by an official body within sufficient legal power to enforce it
- It should be widely published and accepted
- Have clear and specific definitions/descriptions of critical elements
- It processes should be clear and fair...”<sup>286</sup>

The mandate of the NHREC and its CADC, as well as its guidelines for the management of complaints are conceptually sound and consistent with international best practice guidelines, and with the conditions proposed by Lock *et al*.<sup>287</sup> In its 2014-2015 Annual Report, the NHREC reported that the CADC only handled three complaints during this period.<sup>288</sup> The author of this paper is of the opinion that this figure is extremely low, and not a true reflection of the prevalence of research misconduct in South Africa. This low figure might suggest that the bulk of research misconduct cases were resolved at an institutional level (by RECs) without the intervention of the CADC, or perhaps, the existence, duties and functions of the CADC are not well recognised in the research community.

### 3.9 CONCLUDING REMARKS

All members of the scientific community are morally and professionally obliged to report suspected cases of misconduct to the relevant authorities. This chapter highlighted the various forms of research misconduct; highlighted preventative strategies aimed at curbing

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<sup>284</sup> UK Research Integrity Office "Procedure for the Investigation of Misconduct in Research" (2008) 26.

<sup>285</sup> As referenced in Giannobile *et al* (2010) 70; Lock *et al* (2001) "Fraud and Misconduct: in Biomedical Research" 27-28.

<sup>286</sup> Lock *et al* (2001) 27-28.

<sup>287</sup> The Organisation for Economic Co-operation and Development (OECD) Global Science Forum "Best Practices for Ensuring Scientific Integrity and Preventing Misconduct" (2007) 9-11; Lock *et al* (2001) 27-28; UK Research Integrity Office "Procedure for the Investigation of Misconduct in Research" (2008) 21-26.

<sup>288</sup> Department of Health "National Health Research Ethics Committee Annual Report (2014-2015)" 12.

research misconduct; and briefly discussed the regulatory framework for dealing with research misconduct allegations.

A first-hand experience that the author encountered in the process of writing up this dissertation must be mentioned. While conducting a review of the literature, the author stumbled upon a Croatian study by Marušić *et al* titled “A systematic review of research on the meaning, ethics and practices of authorship across scholarly disciplines”, published in *PLOS Medicine* in 2011. In this systematic review, Marušić *et al* reported a 64% rate of problems with, misuse of authorship in South Africa,<sup>289</sup> citing a study by Gina Joubert titled, “Practices and experiences in the Faculty of Health Sciences of the University of the Free State”, published in the *South African Family Practice* in 2005. Upon acquiring and reading Joubert’s article however, it was discovered that Joubert actually concluded the opposite: “No problems were experienced regarding authorship in relation to 64% of the papers”<sup>290</sup> To make matters worse, a Nigerian study by Ana *et al* titled “Research misconduct in low-and middle-income countries”, also published in *PLOS Medicine* in 2013, stated that South Africa reported an authorship misuse rate of 64%<sup>291</sup> citing the Marušić review. Regardless of whether Marušić *et al*’s inaccuracy was due to honest error or not, its consequences are far reaching. The author of this dissertation, however, managed to contact Gina Joubert (who agreed that the findings of her study were indeed misrepresented) and advised her to follow up the matter with the journal, so that a thorough investigation may be conducted.

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<sup>289</sup> Marušić *et al* "A systematic review of research on the meaning, ethics and practices of authorship across scholarly disciplines" (2011) 6, 9 *PloS one* e23477.

<sup>290</sup> Joubert "Authorship: practices and experiences in the Faculty of Health Sciences of the University of the Free State" (2005) 47, 4 *SA Fam Pract* 57-60.

<sup>291</sup> Ana *et al* (2013) 10, 3 *PLoS Med* 1-5.

## CHAPTER 4: CONCLUSION

“While patient autonomy, informed consent, confidentiality, protection of privacy, professional competence, standards of care and rational, sound, scientific evidence are critical components in distinguishing between acceptable and unacceptable healthcare research, the determination is ultimately an ethical one and comes down to preparedness, clarity, transparency, and respect for human rights and justice.”<sup>292</sup>

Scientists like all other professionals are susceptible to pressures and temptations.<sup>293</sup> This, may result in them engaging in questionable research practices or deliberate misconduct.<sup>294</sup> However, we all have an inherent moral compass that allows us human beings to differentiate between right and wrong. However, there are instances where the lines become blurry, and there is no absolute right or wrong. When faced with such moral dilemmas, this inherent moral compass must be used in conjunction with the four key ethical principles used in bioethics to make an ethically sound decision.

Research misconduct is a real problem that is plaguing the scientific community. The damage that it inflicts on the integrity and credibility of the scientific record, and on public health and opinion is detrimental and extremely difficult to remedy. As discussed in this dissertation, strategies to fight this scourge should be aimed at preventing misconduct, rather than at repairing the damage it inflicts. The following critical topics were briefly discussed: the applicable statutes, regulations and guidelines that govern biomedical research both nationally and internationally; the complexities associated with research involving human participants; the common forms of research misconduct; strategies aimed at promoting and reinforcing research integrity and responsible publication ethics; and current policies\guidelines relating to the management of research misconduct in South Africa.

By sensitizing the readers to the grave problem of research misconduct, the author hopes to have contributed in a small way to the preservation of the scientific record.

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<sup>292</sup> Moodley (2011) 336.

<sup>293</sup> The Organisation for Economic Co-operation and Development Global Science Forum "Best Practices for Ensuring Scientific Integrity and Preventing Misconduct" (2007) 5.

<sup>294</sup> *Ibid.*

## APPENDIX A

**TABLE 1. APPLICABLE INTERNATIONAL REGULATIONS, GUIDELINES AND CODES RELATING TO BIOMEDICAL RESEARCH ON HUMANS**

Policies/Guidelines/Codes	Version /Last Updated	Available online at:	Date Accessed
<b>INTERNATIONAL</b>			
The Nuremberg Code	1947	<a href="http://www.hhs.gov/ohrp/archive/nurember.html">http://www.hhs.gov/ohrp/archive/nurember.html</a>	29-03-2016
The Belmont Report	1979	<a href="http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html">http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html</a>	29-03-2016
World Medical Association is the Declaration of Helsinki	2013	<a href="http://www.wma.net/en/30publications/10policies/b3/index.html">http://www.wma.net/en/30publications/10policies/b3/index.html</a>	29-03-2016
CIOMS in collaboration with WHO, International Ethical Guidelines for Biomedical Research Involving Human Subjects	2002	<a href="http://www.cioms.ch/publications/layout_guide2002.pdf">http://www.cioms.ch/publications/layout_guide2002.pdf</a>	29-03-2016
WHO Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products	1995	<a href="http://apps.who.int/medicinedocs/pdf/whozip13e/whozip13e.pdf">http://apps.who.int/medicinedocs/pdf/whozip13e/whozip13e.pdf</a>	29-03-2016
WHO Handbook for Good Clinical Research Practice (GCP)	2005	<a href="http://apps.who.int/iris/bitstream/10665/43392/1/924159392X_eng.pdf">http://apps.who.int/iris/bitstream/10665/43392/1/924159392X_eng.pdf</a>	29-03-2016
WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants	2011	<a href="http://apps.who.int/iris/bitstream/10665/44783/1/9789241502948_eng.pdf?ua=1">http://apps.who.int/iris/bitstream/10665/44783/1/9789241502948_eng.pdf?ua=1</a>	29-03-2016
CIOMS International Ethical Guidelines for Epidemiological Studies	2009	<a href="https://www.ufrgs.br/bioetica/cioms2008.pdf">https://www.ufrgs.br/bioetica/cioms2008.pdf</a>	29-03-2016



ICH Guidelines for Good Clinical Practice, ICH Harmonised Tripartite Guideline	1996	<a href="http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf">http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf</a>	29-03-2016
The Nuffield Council on Bioethics', The ethics of research related to healthcare in developing countries	2002	<a href="http://nuffieldbioethics.org/wp-content/uploads/2014/07/Ethics-of-research-related-to-healthcare-in-developing-countries-1.pdf">http://nuffieldbioethics.org/wp-content/uploads/2014/07/Ethics-of-research-related-to-healthcare-in-developing-countries-1.pdf</a>	30-03-2016
The Nuffield Council on Bioethics', The ethics of research related to healthcare in developing countries: a follow-up discussion paper	2005	<a href="http://nuffieldbioethics.org/wp-content/uploads/2014/07/HRRDC_Follow-up_Discussion_Paper.pdf">http://nuffieldbioethics.org/wp-content/uploads/2014/07/HRRDC_Follow-up_Discussion_Paper.pdf</a>	30-03-2016
Sample Policy and Procedures for Responding to Allegations of Research Misconduct	2005	<a href="http://ori.dhhs.gov/sample-policy-procedures-responding-research-misconduct-allegations">http://ori.dhhs.gov/sample-policy-procedures-responding-research-misconduct-allegations</a>	18-09-2016





**TABLE 2. APPLICABLE STATUTES, REGULATIONS, GUIDELINES AND CODES RELATING TO BIOMEDICAL RESEARCH ON HUMANS IN SOUTH AFRICA**

Statutes/Regulations/ Guidelines/Codes	Version /Last Updated	Available online at:	Date Accessed
<b>NATIONAL</b>			
Sections 12 and 16 of the Constitution of the Republic of South Africa	1996	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
The National Health Act 61 of 2003	2003	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Government Notice R719 Regulations relating to research with human Participants, published in Government Gazette 38000	2014	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Government Notice R839 Regulations relating to the National Health Research Ethics Council in Government Gazette 33574	2010	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Government Notice R840 Regulations relating to the establishment of the National Health Research Committee published in Government Gazette 33575	2010	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Government Notice R177 Regulations relating to the use of Human Biological Material in Government Gazette 35099	2012	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Government Notice R180 Regulations Regarding the General Control Of Human Bodies, Tissue, Blood, Blood products and Gametes in Government Gazette 35099	2012	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016



Government notice R182 Regulations relating to tissue banks in Government Gazette 35099	2012	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Government notice R183 Regulations relating to stem cell banks in Government Gazette 35099	2012	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Government notice R636 Regulations regarding the rendering of forensic pathology service in Government Gazette 30110	2007	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Children's Act 38 of 2005	2005	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Protection of Personal Information Act 4 of 2013	2013	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Mental Health Care Act 17 of 2002	2002	<a href="http://www.justice.gov.za/legislation/acts/2002-017_mentalhealthcare.pdf">http://www.justice.gov.za/legislation/acts/2002-017_mentalhealthcare.pdf</a>	29-03-2016
Medicines and Related Substances Control Act 101 of 1965	1965	<a href="http://www.lawsouthafrica.up.ac.za/index.php/current-legislation">http://www.lawsouthafrica.up.ac.za/index.php/current-legislation</a>	29-03-2016
Health Professions Act 56 of 1974 and associated government notice R717 Ethical rules of conduct for practitioners registered under the Health Professions Act, 1974	1974	<a href="http://www.hpcs.co.za/Uploads/editor/UserFiles/downloads/legislations/acts/health_professions_ct_56_1974.pdf">http://www.hpcs.co.za/Uploads/editor/UserFiles/downloads/legislations/acts/health_professions_ct_56_1974.pdf</a>	29-03-2016
The National Department of Health's Ethics in Health Research, 2nd edition	2015	<a href="http://www.nhrec.org.za/docs/Documents/EthicsHealthResearchFinalAused.pdf">http://www.nhrec.org.za/docs/Documents/EthicsHealthResearchFinalAused.pdf</a>	29-03-2016
Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa, 1st edition	2000	<a href="http://www.kznhealth.gov.za/research/guideline2.pdf">http://www.kznhealth.gov.za/research/guideline2.pdf</a>	29-03-2016
The South African Good Clinical Practice Guidelines, 2nd edition	2006	<a href="http://www.kznhealth.gov.za/research/guideline1.pdf">http://www.kznhealth.gov.za/research/guideline1.pdf</a>	29-03-2016



MRC's Guidelines on ethics for medical research (Series -Books 1 to 5)	2002-2004	<a href="http://www.mrc.ac.za/ethics/ethics.htm">http://www.mrc.ac.za/ethics/ethics.htm</a>	29-03-2016
HPCSA's Guidelines for Good Practice in the Health Care Professions, Booklet 6:General Ethical Guidelines for Health Researchers	2008	<a href="http://www.hpcsa.co.za/conduct/Ethics">http://www.hpcsa.co.za/conduct/Ethics</a>	29-03-2016
NHREC and CADC: Guideline for the Management of Complaints	2015	<a href="http://www.nhrec.org.za/docs/Documents/FinalNHRECGuidelinemanagementcomplaintsrevised.pdf">http://www.nhrec.org.za/docs/Documents/FinalNHRECGuidelinemanagementcomplaintsrevised.pdf</a>	20-09-2016



**TABLE 3. IMPORTANT GUIDELINES AND POLICIES ON GOOD PUBLICATION PRACTICE**

<b>Guideline/Policy</b>	<b>Version/ Last Updated</b>	<b>Available online at:</b>	<b>Date Accessed</b>
COPE's Guidelines on good publication practice	1999	<a href="http://publicationethics.org/files/u7141/1999pdf13.pdf">http://publicationethics.org/files/u7141/1999pdf13.pdf</a>	29-08-2016
COPE's How to handle authorship disputes: a guide for new researchers	2003	<a href="http://publicationethics.org/files/2003pdf12_0.pdf">http://publicationethics.org/files/2003pdf12_0.pdf</a>	29-08-2016
COPE's Retraction Guidelines	2009	<a href="http://publicationethics.org/files/retraction%20guidelines.pdf">http://publicationethics.org/files/retraction%20guidelines.pdf</a>	26-08-2016
COPE's Various flowcharts on dealing with E-seminars on handling suspected research and publication misconduct	n/a	<a href="http://publicationethics.org/resources">http://publicationethics.org/resources</a>	29-08-2016
International Society for Medical Publication Professionals: Good publication practice for communicating company sponsored medical research: the GPP2 guidelines	2009	<a href="http://www.bmj.com/content/339/bmj.b4330">http://www.bmj.com/content/339/bmj.b4330</a>	29-08-2016
International Society for Medical Publication Professionals: Good Publication Practice for Communicating Company-Sponsored Medical Research: GPP3	2015	<a href="http://annals.org/article.aspx?articleid=2424869">http://annals.org/article.aspx?articleid=2424869</a>	29-08-2016
Avoiding plagiarism, self-plagiarism, and other questionable writing practices: A guide to ethical writing by Miguel Roig. (Posted on the Office of Research Integrity website)	2011	<a href="http://ori.hhs.gov/avoiding-plagiarism-self-plagiarism-and-other-questionable-writing-practices-guide-ethical-writing">http://ori.hhs.gov/avoiding-plagiarism-self-plagiarism-and-other-questionable-writing-practices-guide-ethical-writing</a>	29-08-2016
WAME's Recommendations on Publication Ethics Policies for Medical Journals	2016	<a href="http://www.wame.org/about/recommendations-on-publication-ethics-police">http://www.wame.org/about/recommendations-on-publication-ethics-police</a>	29-08-2016
ICMJE's Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals	2015	<a href="http://www.icmje.org/recommendations/">http://www.icmje.org/recommendations/</a>	30-08-2016
The Office of Research Integrity Website: Various E-Seminars, online modules and guidelines relating to publication ethics and research misconduct.	2016	<a href="http://ori.hhs.gov/">http://ori.hhs.gov/</a>	29-08-2016

**FIGURE 1. THE SINGAPORE STATEMENT** <sup>295</sup>

## Singapore Statement on Research Integrity

**Preamble.** The value and benefits of research are vitally dependent on the integrity of research. While there can be and are national and disciplinary differences in the way research is organized and conducted, there are also principles and professional responsibilities that are fundamental to the integrity of research wherever it is undertaken.

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### PRINCIPLES

*Honesty* in all aspects of research  
*Accountability* in the conduct of research  
*Professional courtesy and fairness* in working with others  
*Good stewardship* of research on behalf of others

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### RESPONSIBILITIES

<p><b>1. Integrity:</b> Researchers should take responsibility for the trustworthiness of their research.</p> <p><b>2. Adherence to Regulations:</b> Researchers should be aware of and adhere to regulations and policies related to research.</p> <p><b>3. Research Methods:</b> Researchers should employ appropriate research methods, base conclusions on critical analysis of the evidence and report findings and interpretations fully and objectively.</p> <p><b>4. Research Records:</b> Researchers should keep clear, accurate records of all research in ways that will allow verification and replication of their work by others.</p> <p><b>5. Research Findings:</b> Researchers should share data and findings openly and promptly, as soon as they have had an opportunity to establish priority and ownership claims.</p> <p><b>6. Authorship:</b> Researchers should take responsibility for their contributions to all publications, funding applications, reports and other representations of their research. Lists of authors should include all those and only those who meet applicable authorship criteria.</p> <p><b>7. Publication Acknowledgement:</b> Researchers should acknowledge in publications the names and roles of those who made significant contributions to the research, including writers, funders, sponsors, and others, but do not meet authorship criteria.</p> <p><b>8. Peer Review:</b> Researchers should provide fair, prompt and rigorous evaluations and respect confidentiality when reviewing others' work.</p> <p><b>9. Conflict of Interest:</b> Researchers should disclose financial and other conflicts of interest that could compromise the trustworthiness of their work in research proposals, publications and public communications as well as in all review activities.</p>	<p><b>10. Public Communication:</b> Researchers should limit professional comments to their recognized expertise when engaged in public discussions about the application and importance of research findings and clearly distinguish professional comments from opinions based on personal views.</p> <p><b>11. Reporting Irresponsible Research Practices:</b> Researchers should report to the appropriate authorities any suspected research misconduct, including fabrication, falsification or plagiarism, and other irresponsible research practices that undermine the trustworthiness of research, such as carelessness, improperly listing authors, failing to report conflicting data, or the use of misleading analytical methods.</p> <p><b>12. Responding to Irresponsible Research Practices:</b> Research institutions, as well as journals, professional organizations and agencies that have commitments to research, should have procedures for responding to allegations of misconduct and other irresponsible research practices and for protecting those who report such behavior in good faith. When misconduct or other irresponsible research practice is confirmed, appropriate actions should be taken promptly, including correcting the research record.</p> <p><b>13. Research Environments:</b> Research institutions should create and sustain environments that encourage integrity through education, clear policies, and reasonable standards for advancement, while fostering work environments that support research integrity.</p> <p><b>14. Societal Considerations:</b> Researchers and research institutions should recognize that they have an ethical obligation to weigh societal benefits against risks inherent in their work.</p>
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The Singapore Statement on Research Integrity was developed as part of the 2nd World Conference on Research Integrity, 21-24 July 2010, in Singapore, as a global guide to the responsible conduct of research. It is not a regulatory document and does not represent the official policies of the countries and organizations that funded and/or participated in the Conference. For official policies, guidance, and regulations relating to research integrity, appropriate national bodies and organizations should be consulted. Available at: [www.singaporestatement.org](http://www.singaporestatement.org)

<sup>295</sup> 2nd World Conference on Research Integrity web page "Singapore Statement on Research Integrity" (2010).

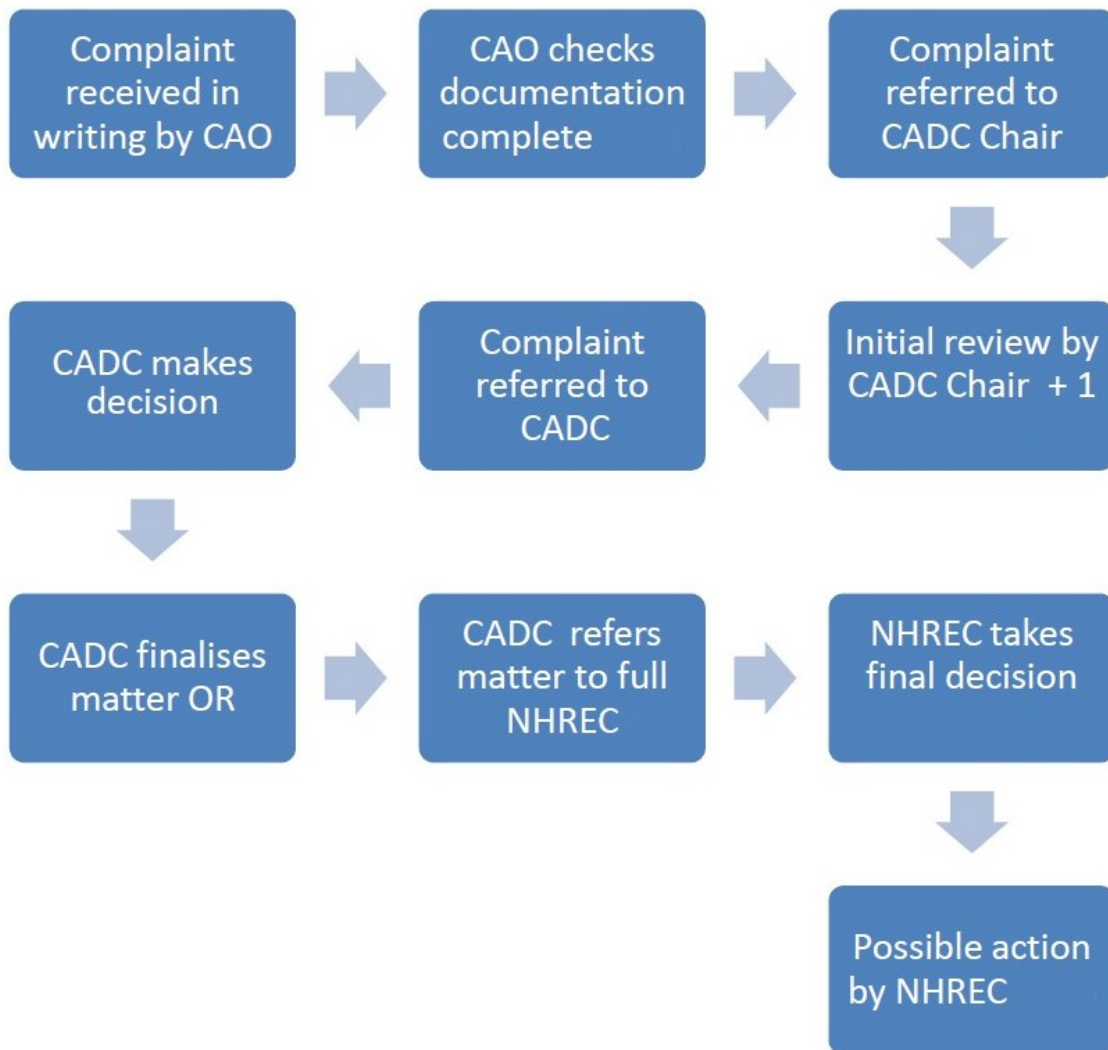
## FIGURE 2. VARIOUS ONLINE SEARCHES CLEARLY DISPLAYING RETRACTION NOTICES

The screenshot shows a Google search for the article title. The search results list the original article and a retraction notice. The retraction notice is circled in red. The text of the retraction notice is: "Retraction: Concomitant suppression of three target genes can explain the impact of a microRNA on metastasis. [Genes Dev. 2015]".

The screenshot shows a PubMed search result for the article. The article title is "Concomitant suppression of three target genes can explain the impact of a microRNA on metastasis." The authors are Valastyan S<sup>1</sup>, Benaich N, Chang A, Reinhardt F, Weinberg RA. The article is marked as a retracted article. The retraction notice is circled in red. The text of the retraction notice is: "Retraction: Concomitant suppression of three target genes can explain the impact of a microRNA on metastasis. [Genes Dev. 2015]".

The screenshot shows the Genes & Development journal website. The article title is "Concomitant suppression of three target genes can explain the impact of a microRNA on metastasis". The authors are Scott Valastyan, Nathan Benaich, Amelia Chang, Ferenc Reinhardt and Robert A. Weinberg. The article is marked as a retracted article. The retraction notice is circled in red. The text of the retraction notice is: "Retraction".

**FIGURE 3. FLOWCHART OUTLINING THE COMPLAINTS PROCESS FOLLOWED BY THE CADC** <sup>296</sup>



<sup>296</sup> Adapted from National Health Research Ethics Council's Complaints and Advisory Disciplinary Committee "Guideline for the Management of Complaints" (2015) 10.

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